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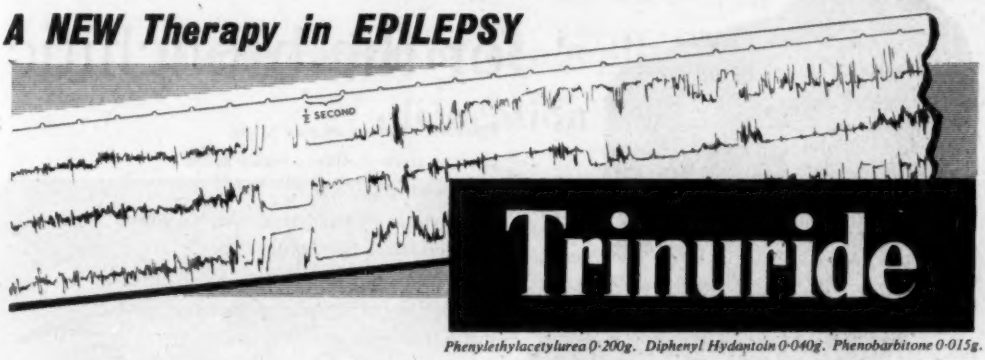

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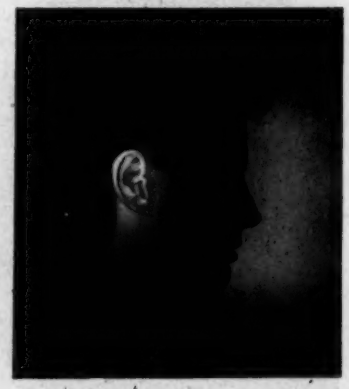

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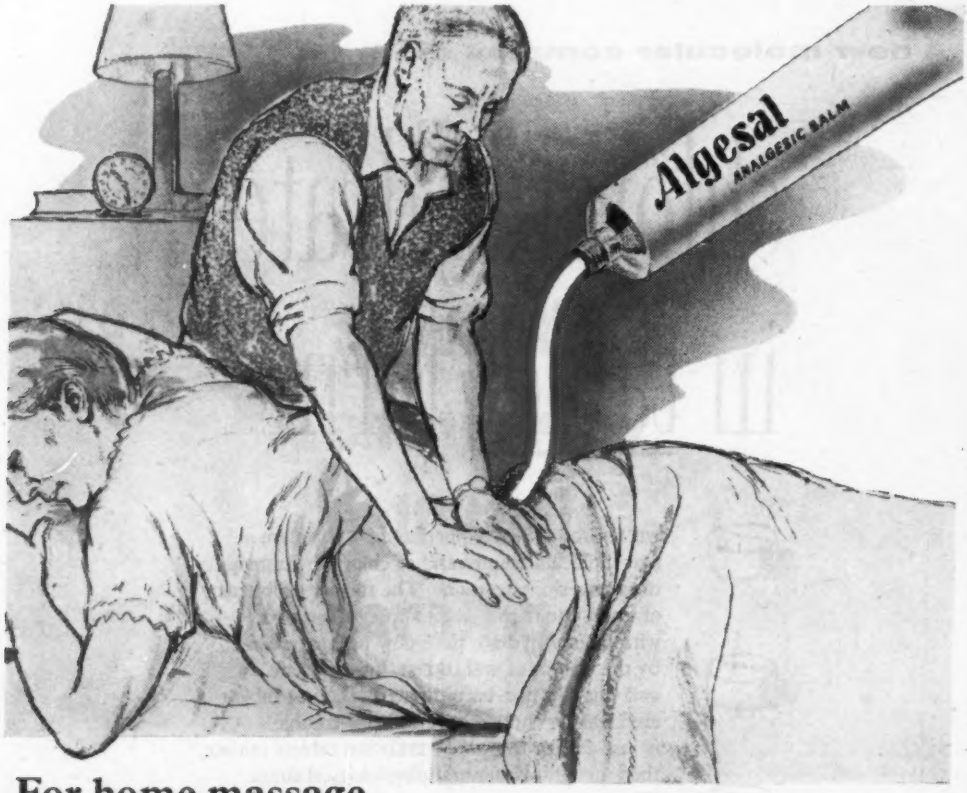

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Medical literature is available on request

Neophryn gives relief without secondary congestion

Trade Mark

Neophryn is a sympathomimetic amine (l-m-hydroxy-α-methylaminomethyl benzyl alcohol HCl) in aqueous solution; available as a spray or drops

Basic N.H.S. cost of Nasal Spray or Drops 2/4. With antihistamine (in spray form only): 2/8

Bayer Products Limited
Neville House, Kingston-on-Thames, Surrey.
Associated exporting company: Winthrop Products Limited

BAYER

a complex need

STRENGTH?

LOTION?

OR OINTMENT?

GREASY?

OR NON-GREASY?

a simple answer

CORTRIL TOPICAL OINTMENTS

Greasy: 1.0% and 2.5%.
Non-Greasy: 0.5%, 1.0% and 2.5%.
Both in tubes of 5 g. and 15 g.

CORTRIL LOTION

0.5% and 1.0%
in 20 ml. bottles.

Cortril*
brand of hydrocortisone

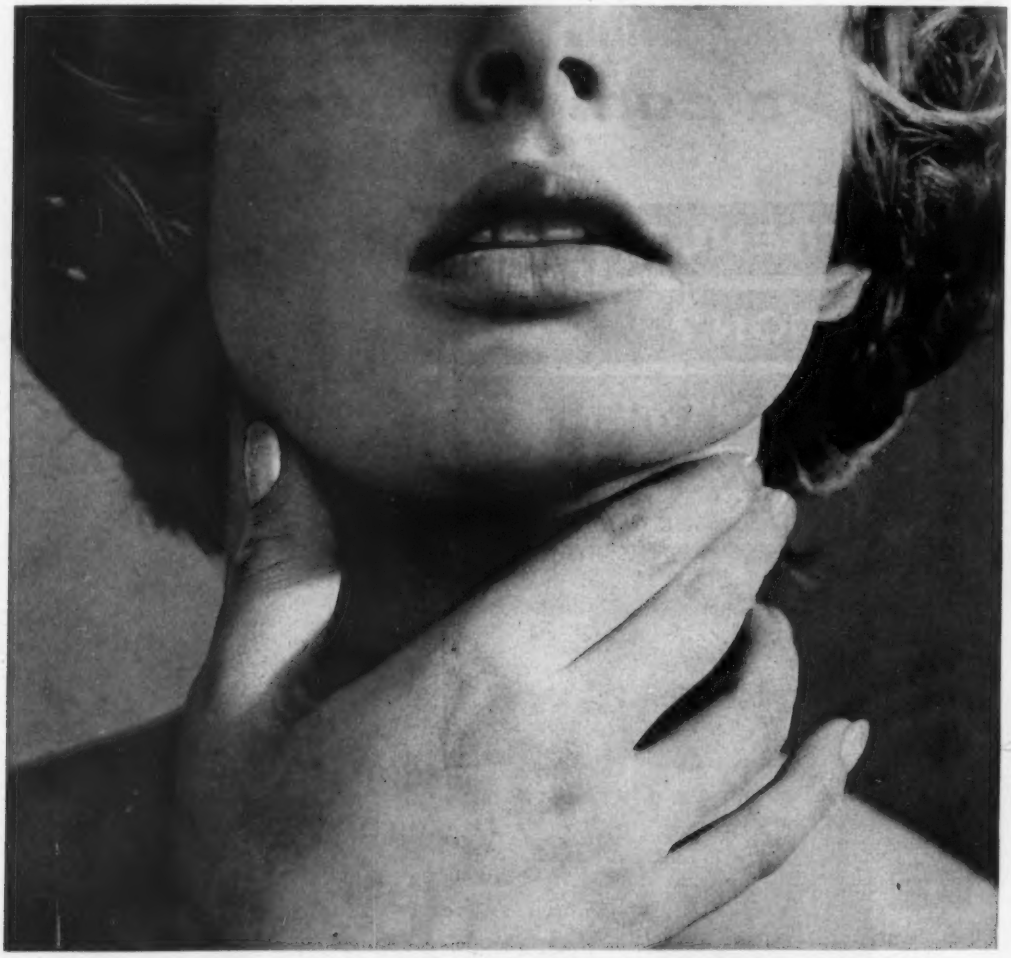
IN ALL NON-INFECTED DERMATOSES

PFIZER PHARMACEUTICALS
Manufactured at Sandwich and Processed at Folkestone, Kent

* *Registered Trade Mark*

Pfizer

072/P



For the prevention and treatment of infections of the mouth and throat

SALIVA TESTS prove that 'Hibitane' Lozenges are more active in the mouth than other antiseptic lozenges. When 'Hibitane' Lozenges are sucked at 2-hourly intervals the oral streptococcal counts show up to a one-hundred-fold reduction.

'Hibitane' Lozenges each contain 5 mg. 'Hibitane' chlorhexidine Dihydrochloride, with 2 mg. Benzocaine B.P.—sufficient to ease pain without interfering with the swallowing reflex or hindering healing.

Noteworthy characteristics

Powerful antibacterial effect; safe; bacterial resistance cannot be induced; pleasantly flavoured and well liked by children.

'Hibitane' *antiseptic lozenges*

Available in tubes of 12 *lozenges*

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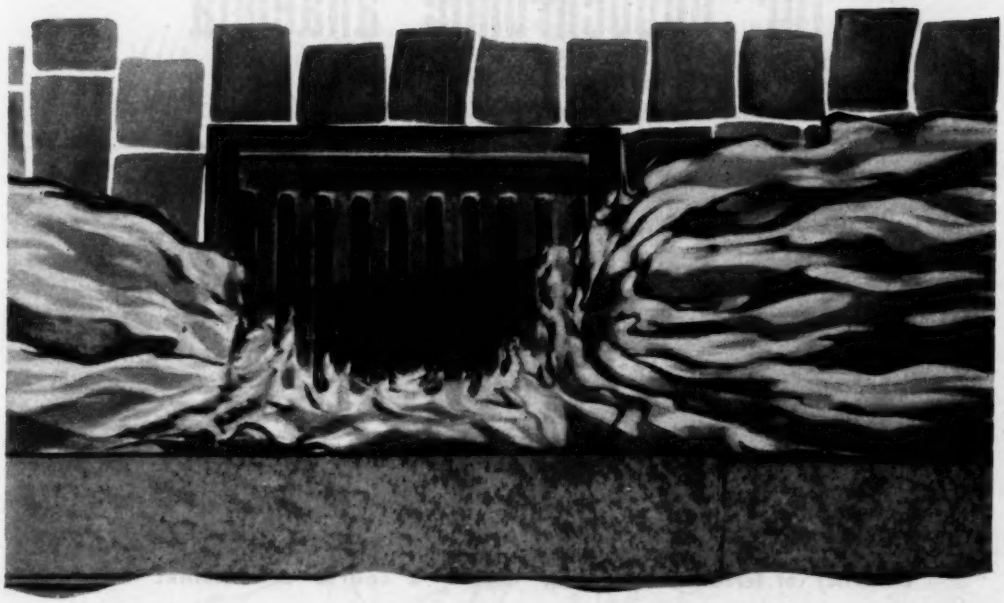
IMPERIAL CHEMICAL INDUSTRIES LIMITED Pharmaceuticals Division Wilmslow Cheshire

PH.789

Keeping the fluid level under control



DIAMOX Acetazolamide is now established as the rational choice among diuretics. From the patient's viewpoint, DIAMOX is the most convenient of diuretics, being effective orally and giving an unusually rapid response. Equally important, DIAMOX is *safe*. It is non-mercurial, virtually non-toxic, and non-cumulative in body tissues. It is thus suitable for long-term therapy in the control of body fluid.

MAIN INDICATIONS: CARDIAC OEDEMA · GLAUCOMA · EPILEPSY TOXAEMIA AND OEDEMA OF PREGNANCY · PREMENSTRUAL TENSION

DIAMOX*

ACETAZOLAMIDE

* REGD. TRADE MARK

ORAL TABLETS *250 mg. Bottles of 25, 100 and 1,000*

PARENTERAL *Vials of 500 mg. Acetazolamide Sodium*

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LEDERLE LABORATORIES DIVISION

Cyanamid OF GREAT BRITAIN LTD., London, W.C.2

Ideal ferrous sulphate treatment for hypochromic anaemia

Plesmet TABLETS

EXCEPTIONALLY WELL TOLERATED

RAPID ABSORPTION

MAXIMUM UTILISATION

LOW COST

Plesmet improves on hæmopoietic efficiency of ferrous sulphate in all iron deficiency anæmias by ensuring that it is exraordinarily well tolerated — particularly in pregnancy.

EACH TABLET CONTAINS

Ferrous Amino-acetosulphate equivalent to 50 mgm. of Ferrous Iron with 1 mgm. of Aneurine Hydrochloride B.P.

In a recent clinical trial a a course of Plesmet was markedly successful in raising the hæmoglobin percentage from an initial average level of 62 to 73 in two weeks.

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100 tablets .. 2/8
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MAXIMAL EFFICIENCY AT MINIMAL COST- WRITE FOR SAMPLES & LITERATURE

For

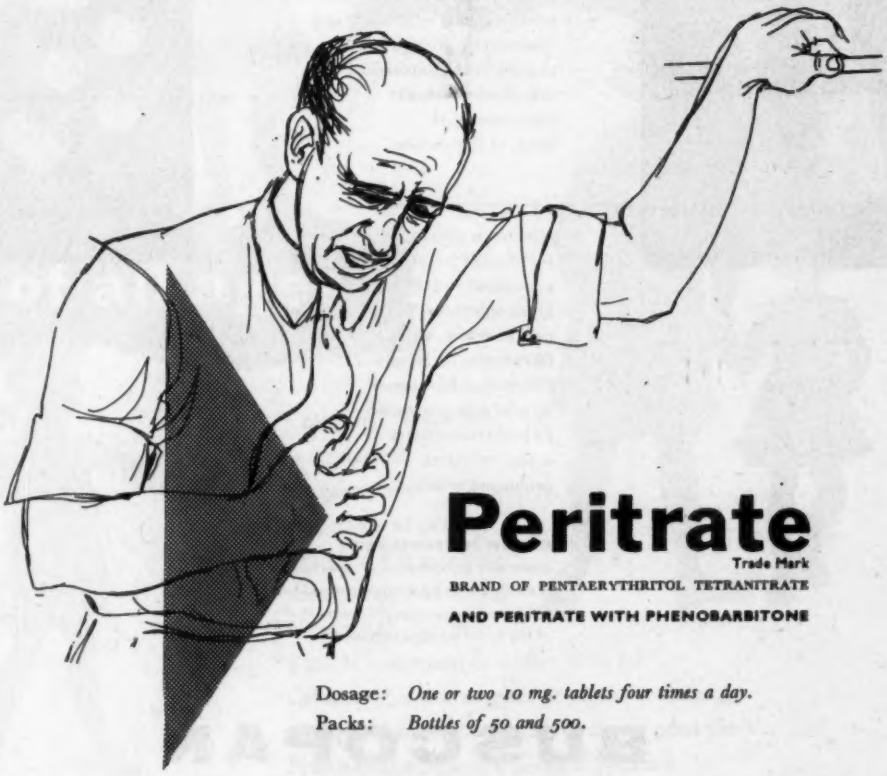
the patient

with angina

Peritrate is a valuable aid in the treatment of angina by virtue of its action as a coronary vasodilator. Each 10 mg. tablet begins to act half-an-hour after ingestion and the action continues 4-5 hours. Peritrate prevents anginal attacks, or reduces their frequency, severity and duration. It diminishes the patient's nitroglycerin requirements, and improves exercise tolerance. Peritrate is non-toxic and causes very few side-effects even on prolonged administration.

PERITRATE WITH PHENOBARBITONE

Peritrate is now available with Phenobarbitone for the Angina Pectoris patient who needs sedation. Each tablet contains 10 mg. Peritrate and 15 mg. Phenobarbitone. The packs and prices for these tablets are the same as for Peritrate.



Peritrate

Trade Mark

BRAND OF PENTAERYTHRITOL TETRANITRATE

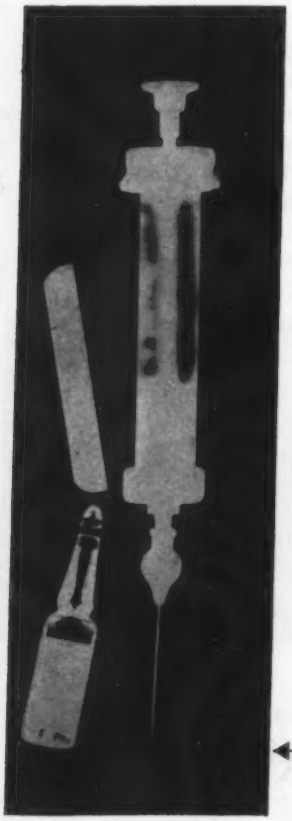
AND PERITRATE WITH PHENOBARBITONE

Dosage: *One or two 10 mg. tablets four times a day.*

Packs: *Bottles of 50 and 500.*

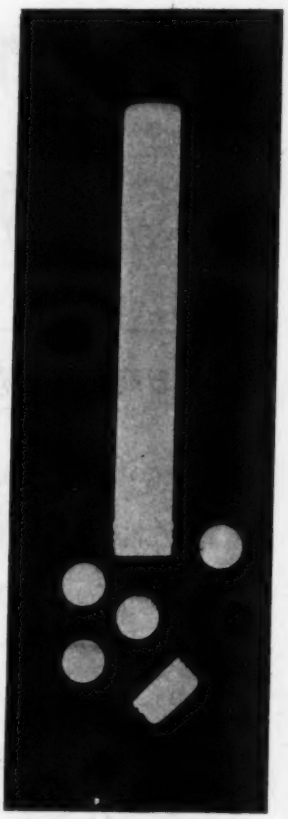
Further information is available on request.

WILLIAM R. WARNER & CO. LTD., EASTLEIGH, HAMPSHIRE.



in cases of spasmodic dysmenorrhoea

Prophylactically, a course of tablets starting a day or two before the expected flow will give



complete relief in most cases. BUSCOPAN is a completely safe spasmolytic giving rise to none of the unpleasant side effects normally associated with drugs of this nature.

BUSCOPAN gives rapid relief from pain associated with Spasmodic Dysmenorrhœa. When pain is severe, an intramuscular injection followed in four hours by oral administration *(2 tablets three times a day)* will give prolonged relief.

Other indications
Gastric or duodenal ulcer, spasmodic disorders of the gastro-intestinal tract, biliary colic and delayed relaxation of the lower uterine segment.

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Hyoscine-N-Butylbromide

Manufactured and distributed in the U.K. by Pfizer, Ltd., Folkestone, Kent, for
C. H. Boehringer Sohn, Ingelheim am Rhein.
Registered Proprietors of the Trade Mark. * *Regd. Trade Mark.*

Calcipen-V SUSPENSION

for children

of all ages

Calcipen-V Suspension is a palatable, *ready-prepared* suspension of calcium-penicillin V, containing the equivalent of 60 mg. of penicillin V in each 5 ml. It is supplied in bottles of 60 ml. Calcipen-V is also supplied as tablets containing the equivalent of 60, 125 or 250 mg. of penicillin V. Professional sample and detailed literature gladly sent on request.

BOOTS PURE DRUG CO. LTD., NOTTINGHAM, ENGLAND

Boots

Obsolete

Gravitational Therapy

in Migraine

"You are old, Father William," the young man said,
"And your hair has become very white;
And yet you incessantly stand on your head—
Do you think, at your age, it is right?"

"In my youth," Father William replied to his son,
"I did it to cure the migraine;*
But now—why, I do it entirely for fun,
And take Cafergot when I'm in pain."

Cafergot

BY SANDOZ

aborts the attack of migraine in more than 80% of cases

1 mg. Ergotamine Tartrate B.P. 100 mg. Caffeine B.P.	TABLETS
2 mg. Ergotamine Tartrate B.P. 100 mg. Caffeine B.P. 0.25 mg. total alkaloids of belladonna 100 mg. *iso*butylallyl barbituric acid	SUPPOSITORIES

* Standing on one's head is reputed to be a good cure for migraine[1]—but not every patient is so agile.

[1] *Brit. med. J.* (1957) 2, 633

Sandoz Products Limited

Sandoz House
23 Great Castle Street
London, W.1

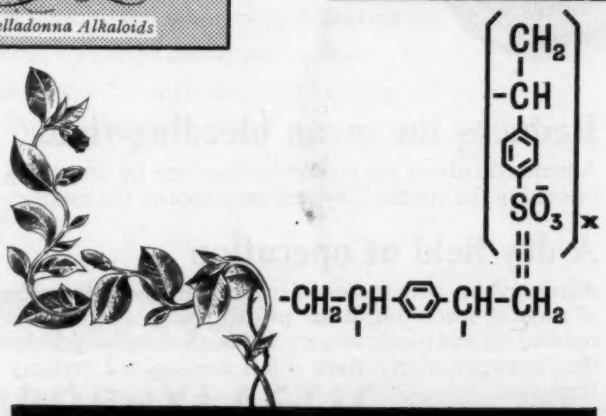
XII

Old

Belladonna Alkaloids

new

ion-exchange resin



IX III

spastipax

oral depot tablets

for

round the clock

spasmolysis

VI

formula: atropine sulph. (0.05 mg.), hyoscyamine sulph. (0.35 mg.), and hyoscine hydrobrom. (0.025 mg.), in optimal proportions plus amylobarbitone (65 mg.); all bonded to ion-exchange resins.

advantages: slow release of active ingredients, 12-hour optimal blood levels, greatly diminished side effects, convenient night and morning dosage, economy.

indications: peptic ulceration, spastic colitis, spasmodic dysmenorrhoea, urinary tract colic, etc., etc.

dosage: ½—2 tablets morning and night. **Basic N.H.S. cost:** 5/- for 30 tablets.

first in the field of oral depot therapy — CPL

'Spastipax' is a 'CPL' registered trade mark

clinical samples and literature sent on request

Medical Dept., Clinical Products Ltd., Richmond, Surrey

ADRENOXYL

Reduces the mean bleeding-time

Adrenoxyl reduces the mean bleeding-time by decreasing the permeability and increasing the contractility and resistance of the capillary wall.

A dry field at operation

Adrenoxyl has been successful in diminishing capillary bleeding in a wide range of surgical operations. It has proved particularly useful in ear, nose and throat, ophthalmic and plastic surgery. In plastic surgery of the face it has been reported that, post-operatively, there is less swelling and bruising when Adrenoxyl has been used.

No side effects

Adrenoxyl does not have any side effects or contraindications. It does not affect blood coagulation, blood pressure or pulse rate and does not possess any sympathomimetic properties.

In medical conditions

Adrenoxyl has been used with success in those medical conditions associated with capillary fragility.

In the British Medical Journal (April 21st, 1956) a correspondent confirmed the value of Adrenoxyl in providing a dry field for the surgeon and in shortening the duration of the operation.

Packs

Ampoules: Boxes of 6 and boxes of 50.
Each ampoule contains 0.75 mg. of adrenochrome monosemicarbazone dihydrate.

Tablets: Tubes of 25 and bottles of 500.
Each tablet contains 2.5 mg. of adrenochrome monosemicarbazone dihydrate.

The best results are obtained when both tablets and ampoules are used.

HORLICKS LIMITED

Pharmaceutical Division Slough Bucks

Literature and samples are available on request to the Medical Information Dept.

Mineral-free

DIPHTHERIA-PERTUSSIS PROPHYLACTIC

The outstanding advantage of this combined prophylactic—in buffered saline—is that, being without mineral carrier, it produces *minimal local reactions*. Three injections of this preparation yield a virtually 100% Schick conversion rate.

and

TRIPLE PROPHYLACTIC

Diphtheria-Tetanus-Pertussis Prophylactic is a combination of Whooping Cough Vaccine, with purified Diphtheria Toxoid *plus* Tetanus Toxoid. The addition of the third Antigen in this preparation now makes possible the protection of children against three common dangers without the need for additional injections.

DIPHTHERIA-TETANUS-PERTUSSIS PROPHYLACTIC

In sets of 3×1 *c.c. doses and in* 10 *c.c. vials.*
Each dose (1 *c.c.*) *contains:*

Purified Diphtheria Toxoid (Formol Toxoid)	25 Lf. Units
Purified Tetanus Toxoid	5 Lf. Units
H. Pertussis (Bordets bacillus)	20,000 Million
Preservative 0·01% Thiomersalate	

• *Diphtheria-Pertussis Prophylactic and Diphtheria-Tetanus-Pertussis Prophylactic are prepared in the Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London, W.3.*

MEDICAMENTA VERA

Sole Agents

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Children like it... worms don't

One week's treatment with 'Antepar' Elixir is usually sufficient to eradicate *threadworms*. A single dose clears *roundworms* from the gut. Effective without fasting, purging or supporting measures, 'Antepar' acts by paralysing the worms—they are then expelled by normal peristalsis.

'Antepar', the original elixir of piperazine, is well tolerated by patients of all ages. Its pleasant taste is popular with children. Containing piperazine citrate equivalent to 500 mgm. of piperazine in each fluid drachm, 'Antepar' is supplied in bottles of 4 fl. oz. and 20 fl. oz.

'ANTEPAR' ELIXIR

BURROUGHS WELLCOME & CO. (THE WELLCOME FOUNDATION LTD.) **LONDON**

Associated Houses:
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Original Everest Expedition photograph
kindly supplied by the
Swiss Foundation for Alpine Research

On top

Bellergal tablets
were carried
to the summit of Everest
by the members of
the 1956 Swiss Expedition
and widely used to counteract
the psychosomatic effects
of stress at high altitudes.

Bellergal

BY **SANDOZ**

is effective at all levels (central,
sympathetic, parasympathetic)
in the symptomatic treatment
of a wide variety
of psychosomatic disorders.

0.1 mg. total alkaloids of belladonna
0.3 mg. Ergotamine Tartrate B.P.
20 mg. Phenobarbitone B.P.

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These are the advantages of

Calcium B-PAS WANDER

and

B-Pasinah WANDER

in the

Chemotherapy of Tuberculosis

B-PAS (Wander), 4-benzoylamino-2-hydroxybenzoic acid, first introduced by our Research Laboratories in 1948, is the drug of choice in regimens comprising PAS in concurrent therapy.

In the form of its calcium salt, it provides extended bacteriostatic levels, induces only minimal side-effects as compared with sodium PAS, and because of its high acceptability guarantees as far as possible that patients, particularly on domiciliary treatment, do take their medication.

Available in 3.5 g. envelopes and in 1 g. cachets; and as bulk powder.

'B-PASINAH' is available in two convenient forms:

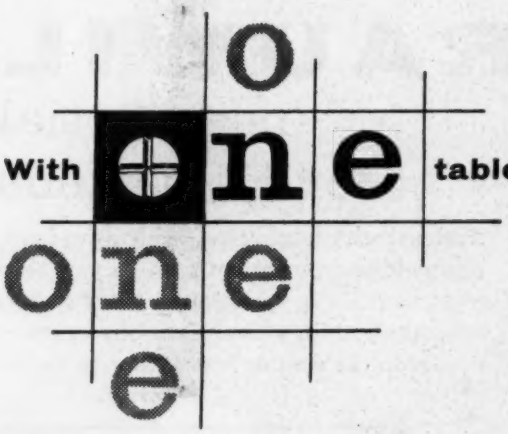
Powders each containing 3.5 g. calcium B-PAS (Wander) and 87.5 mg. isoniazid.

Cachets each containing 1 g. calcium B-PAS (Wander) and 25 mg. isoniazid.

Full abstracts from literature, also details of institutional packs and prices from the Medical Department

A. WANDER LTD., 42 UPPER GROSVENOR ST., GROSVENOR SQ., LONDON W.1

M.400



Midicel

SULPHAMETHOXYPYRIDAZINE

sustained sulphonamide blood-level

prolonged therapeutic effect

The new 'prolonged-action' sulphonamide, MIDICEL*, maintains full therapeutic effect with only one tablet daily. Thus, the patient's comfort and convenience are enhanced and nursing care is simplified.

Comparable in price with other sulphonamides MIDICEL provides added advantage without added cost.

Absorption of MIDICEL is rapid and tissue diffusion is good. In the circulation a high proportion of the contained sulphonamide is in the free active form ensuring full therapeutic action.

Recommended Dosage: In adults an initial loading dose of 1 G (in severe infections only, 2 G) followed by 0.5 G daily. In children ¼ tablet (0.125 G) for each 20 lb. of bodyweight on the first day followed by half this dosage daily.

Packaging: Tablets of 0.5 G in containers of 12, 100 and 250.

*Trade Mark

Parke, Davis HOUNSLOW, MIDDLESEX Tel: HOUnslow 2361

& COMPANY, LTD., (Inc. U.S.A.)

PD.358

'RAUWILOID'

is essential for Hypertension

'Rauwiloid', a purified and standardised fraction of Rauwolfia serpentina alkaloids, can be considered a basic treatment for hypertension. It lowers blood pressure more effectively than phenobarbitone or its combinations with theobromine and is less likely to cause depression than reserpine.

IMPORTANT

'Rauwiloid' may require more than a week for a significant anti-hypertensive effect to develop. Any previous treatment, particularly barbiturate, should be gradually reduced over this period.

In Mild to Moderate Hypertension

In most cases 'Rauwiloid' will provide adequate control by itself. Combination therapy is not necessary.

In Moderate to Severe Hypertension

When a greater hypotensive effect is required, 'Rauwiloid' should be combined with veratrum in the form of 'Rauwiloid + Veriloid'. 'Veriloid' is a biologically standardised alkaloidal extract of Veratrum viride. Such a combination with 'Rauwiloid' enables adequate doses of veratrum to be given for a satisfactory hypotensive response. (See detailed literature).

In Severe or Malignant Hypertension

'Rauwiloid' used in conjunction with ganglionic blocking agents enables a smaller dose of the more potent medicament to be used, thereby minimising side-effects and decreasing the tendency for tolerance to develop.

'Rauwiloid' is available in 2 mg. tablets in bottles of 60 and 500. Dosage, two tablets at night.

RIKER

'Rauwiloid' and 'Veriloid' are registered trade marks

Registered Users

RIKER LABORATORIES LIMITED

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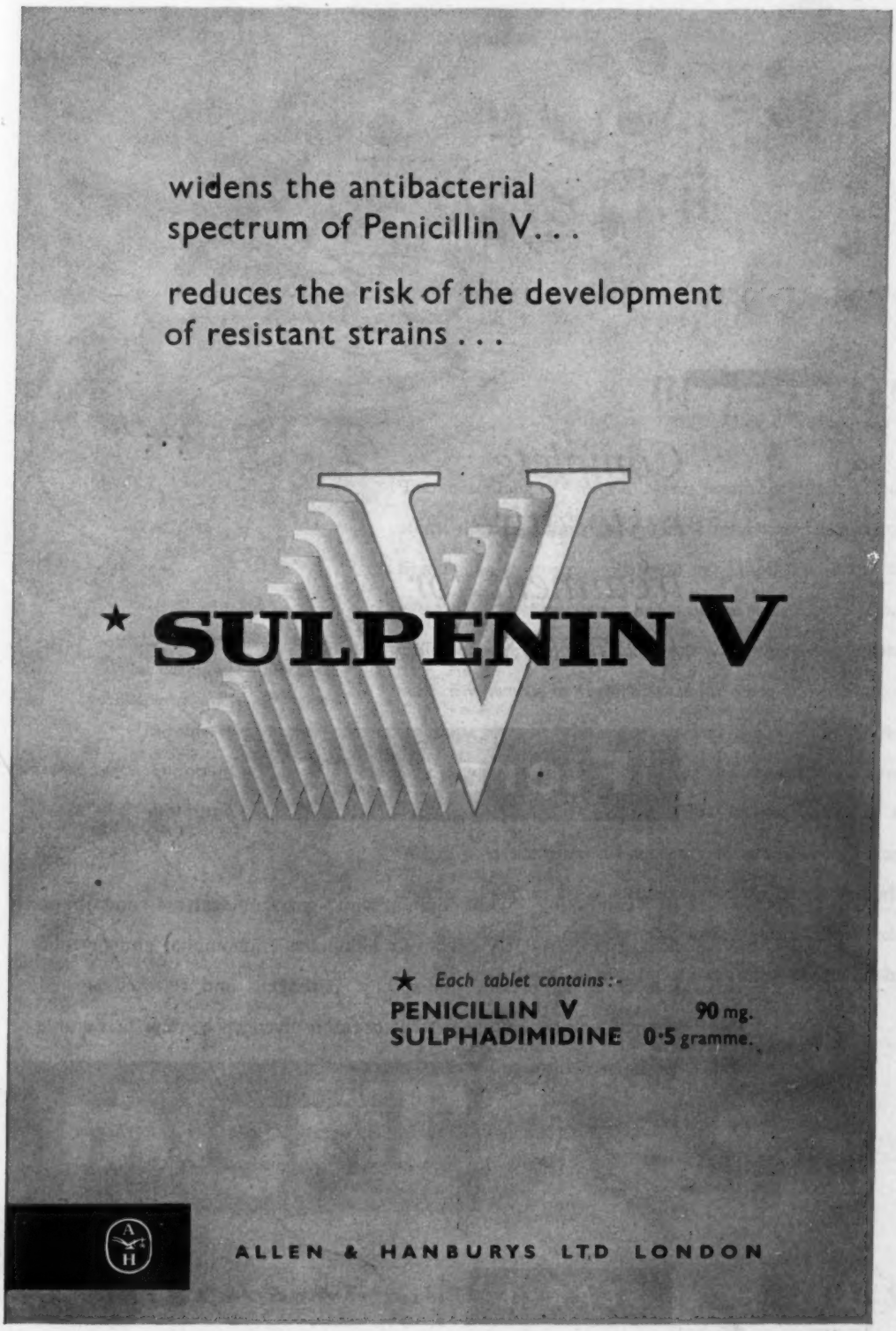
widens the antibacterial
spectrum of Penicillin V...
reduces the risk of the development
of resistant strains...
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★ SULPENIN V
★ Each tablet contains:-
PENICILLIN V 90 mg.
SULPHADIMIDINE 0·5 gramme.
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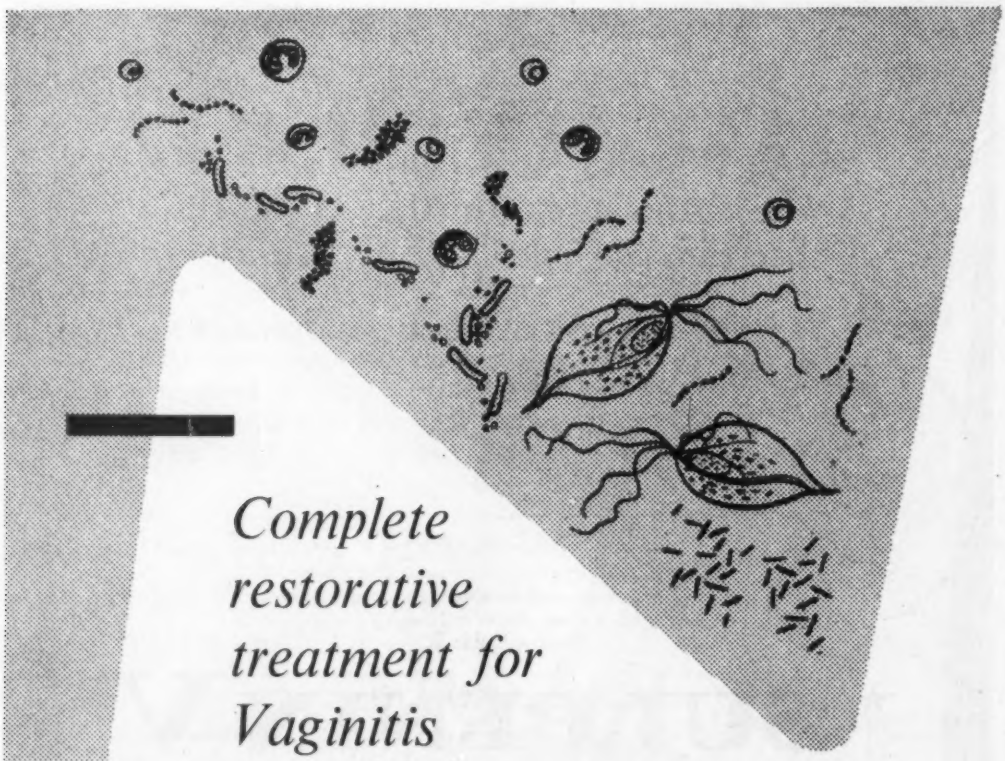
ALLEN & HANBURYS LTD LONDON



Complete restorative treatment for Vaginitis

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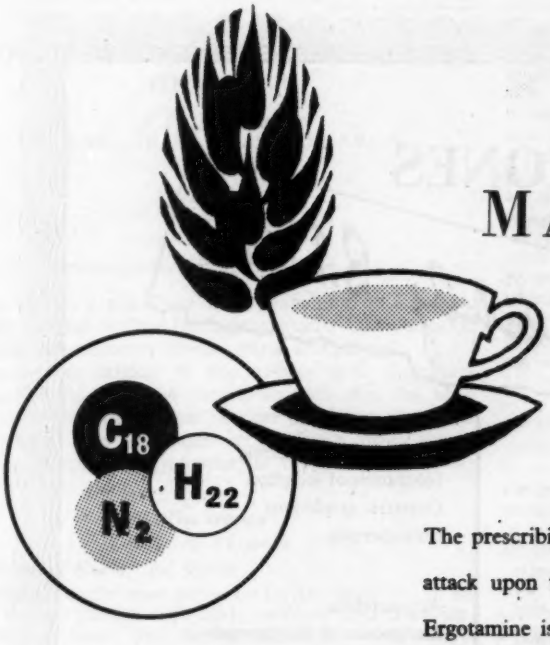
By combining 'Diodoquin' with lactose, dextrose and boric acid, FLORAQUIN effectively eliminates trichomonal and mycotic infections, suppresses non-specific pathogens and restores normal vaginal acidity, epithelial structure and glycogen content favourable to the growth of protective Döderlein bacilli.

Available as tablets in boxes of 25 and 50 with applicator and 400 with 8 applicators, and as powder in 1 oz. bottles.

Literature on request.

SEARLE HIGH WYCOMBE, BUCKS.



today's new MASTER PLAN *against migraine*

Each tablet contains ergotamine tartrate 2 mgm.; caffeine (alkaloid) 100 mgm.; cyclizine hydrochloride 50 mgm.
In bottles of 10 and 100

The prescribing of 'Migril' makes possible at last a *planned* attack upon the three predominant symptoms of migraine. Ergotamine is present at strength in 'Migril' for its specific effect upon the characteristic headache and ocular disturbances. Caffeine is present too, since it acts as a synergist to ergotamine. Frequently, however, ergotamine tends to evoke nausea and vomiting on its own account and can therefore worsen these aspects of the condition. For this reason, the potent, rapidly acting anti-emetic cyclizine is also included in 'Migril'—to overcome any tendency to nausea or vomiting, whether caused by the ergotamine or by the condition itself. And so successfully does cyclizine achieve this aim that truly effective oral doses of ergotamine can today be given—by means of 'Migril'.

'migril' TRADE MARK

BURROUGHS WELLCOME & CO., LONDON
(THE WELLCOME FOUNDATION LTD.)

SEX HORMONES

'Preferably B.D.H.'

'MEPILIN' TRADE MARK Combined androgen—œstrogen	The female climacteric Inhibition of lactation Geriatric conditions Osteoporosis
OESTROGENS	
'ESTIGYN' TRADE MARK 'OESTROFORM' TRADE MARK	Amenorrhœa Carcinoma of the prostate Dysmenorrhœa
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PROGESTIN B.D.H. ETHISTERONE B.D.H. 'LUTOFORM' TRADE MARK	Habitual and threatened abortion Menorrhagia Metrorrhagia Premenstrual tension
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METHYLTESTOSTERONE B.D.H. TESTOSTERONE PROPIONATE B.D.H. 'TESTAFORM' TRADE MARK	Male sterility and impotence Male climacteric Female frigidity Cystic disease of the breast Carcinoma of the breast

For twenty-five years B.D.H. has been a basic producer of Sex Hormones. During that time their utilization has extended enormously and B.D.H. research and manufacturing experience have helped to make their application both practical and economical.

For details of clinical application see booklet, 'B.D.H. Sex Hormones—A clinical review for General Practitioners'

(Medical Department)

THE BRITISH DRUG HOUSES LTD. LONDON

THE PAPILLOMA AND ITS RELATION TO CANCER

Sir CECIL WAKELEY
Bt., K.B.E., C.B., D.Sc. Lond., LL.D., F.R.C.S.
CONSULTING SURGEON

F. T. GRAVES
M.S. Lond., F.R.C.S.
SENIOR SURGICAL REGISTRAR

KING'S COLLEGE HOSPITAL, LONDON, S.E.5

WE define a papilloma as a branching or lobulated benign tumour derived from epithelium. This definition excludes inflammatory lesions, warts, and polypi.

Papillomata arising in the urinary and alimentary tracts, the ducts of the breast, and the skin has been studied to determine what relation they have to cancer. We review here 215 cases of papilloma from King's College Hospital (K.C.H.) seen by the general surgeons from 1948 to 1956.

The Series

PAPILLOMA OF URINARY TRACT

Papilloma of Kidney and Ureter

Papilloma of the renal pelvis constitutes about 3% of all renal tumours (Riches et al. 1951), and only 52% of patients survive five years after having had nephrectomy for it (McDonald and Priestley 1944). We report from K.C.H. 2 cases: in one there were seedling papillomata down the length of the ureter, and the other was associated with a staghorn calculus. Both growths were benign. Papillomatous disease of the renal pelvis is rare and bilateral disease even rarer. One of Macalpine's (1947) patients was a dyeworker thought to have true primary growths on each side and in his bladder. Tumour cells may be found in the urine, and it is important, when carrying out nephro-ureterectomy, not to contaminate the wound, lest implantation take place. Macalpine (1947) found that benign papillomatous material implanted in the wound always became malignant.

Papilloma of the ureter is rare. Moore (1942) noted that less than 60 cases had been reported. We report 3 cases from the K.C.H. series, of which 1 has been mentioned above, and the 2 others were solitary growths at the lower end of the ureter. These conformed, as did those of Wiggins-Davies and Elwood (1952), with the statistical observations of Scott (1943) that these tumours occur most commonly in the lower third of the right ureter.

Papilloma of Bladder and Urethra

The K.C.H. series provided 119 cases: 76% were in males, of whom 60% were over the age of 60; and 24% were in females, of whom 75% were over the age of 60. There were no cases in women under the age of 50. 67% of the growths were close to or at the ureteric orifices, 33% being on the right side and 34% on the left: 11% were near the internal meatus.

Most of these cases followed the usual clinical course of treatment with resultant cure or periodic recurrence. From the remainder come two facts of interest.

Firstly, there were 6 cases which to some extent refute the idea that malignant bladder tumours are always malignant from the outset. In each of these 6 cases biopsy, when the growth was first seen, showed that the tumour was benign. Subsequently, in most cases from three to five years later, biopsy of the recurrent tumour showed it to be malignant. 2 of these cases are of particular interest because, during the period between taking the initial benign biopsy specimen and taking the later malignant biopsy specimen, the tumour recurred—three years after the initial treatment. Further, both simple and malignant recurrences were at or very near the site of the original growth. The second point of interest was that 4 of the cases (3·6%) had coexistent or almost coexistent carcinoma of the sigmoid or the descending colon. These 4 patients were over the age of 60, 3 being women.

Papilloma of the urethra is rare, apart from those on the glans penis, which are probably infective in origin, for they are contagious and spread rapidly after being disturbed by circumcision. Those of the anterior urethra may also be infective. Those of the posterior urethra are transitional-cell tumours and similar to bladder tumours. Some of these may be papilloma seedlings which have become implanted after instrumentation for the treatment of bladder growths (Ashworth 1956). Riches (1944), however, described 3 cases of papilloma in the posterior urethra in which the bladder and upper urinary tracts were clear of growth.

PAPILLOMA OF ALIMENTARY TRACT

Mouth and Pharynx

Although the K.C.H. series is small (7 cases), papillomata on the lips and in the buccal cavity are not uncommon. Mostly the growths are in the middle-aged or the elderly; they are usually single, but are sometimes accompanied by a "kissing" or contact growth, a papilloma on the lower lip having its smaller counterpart on the upper lip, as in 1 of our cases.

Growths of the oropharynx are said to be relatively rare; New and Childrey (1931) reported 35 cases in which the distribution of the growths was almost equal between the fauces, the tonsils, and the soft palate. Similar figures were found by Henner (1942), who reported 94 cases among 25,000 patients examined.

Papilloma of the œsophagus is extremely rare.

Stomach and Small Intestine

The villous papilloma of the stomach, of which there are 51 published cases (Walk 1951), has not been consistently differentiated from the ordinary polyp. Willis (1953) regards the adenoma and the papilloma of the stomach as varieties of the same tumour. Walk found that the incidence of malignancy was high in these villous tumours, the rate of eventual malignancy being highest (72%) in the age-group 61–70. Some of these tumours grew to a considerable size and still showed no evidence of malignant change. These growths not only tend to become malignant but are often associated with carcinoma; in Stewart's (1931) series of 56 stomachs containing benign epithelial tumours, cancer was also present in 27%.

Simple tumours of the small intestine are rare, but the adenoma is the least rare. It is commonly single and more often pedunculated than sessile. Papilloma of the jejunum has presented clinically as melæna and anæmia (Hunnicutt 1952). From a girl of 15, admitted as an emergency, one of us removed a papilloma in a Mackel's diverticulum which had produced an intussusception. A papilloma may arise in heterotopic gastric epithelium in the diverticulum. One such growth was composed of benign adenomatous tissue containing both gastric and duodenal glands (Schullinger and Stout 1934).

Papilloma of Gallbladder

Papilloma of the gallbladder presents often as cholecystitis, sometimes with biliary colic. A cholecystogram often shows a normal gall-bladder as regards function, but there may be a filling defect produced by the papilloma, which is sometimes pedunculated. The biliary colic is attributed to attempted passage of the papilloma down the cystic duct (Lund and Burman 1951). In a case described by Griffiths (1956) the patient had severe biliary colic accompanied by transient jaundice due to obstruction of the common duct by numerous small pieces of growth exuded from the cystic duct.

These papillomata are rare. 8 were found in 2000 cholecystectomies, and coexistent gallstones were found in only 3 of these cases (Kane et al. 1952). Although Mayo (1915) and

Irwin and MacCarty (1915) described a large series of lesions which they considered to be papillomata of the gallbladder, Kerr and Lendrum (1936) suggested that many of these were probably cholesterol polyps.

There is no established view about the relation between papilloma and carcinoma of the gallbladder. Although Shepard et al. (1942) believed that the papillomata rarely became malignant, Tabah and McNeer (1953) hold that papilloma of the gallbladder is a precancerous lesion, and they describe examples of the true papilloma having histological evidence of malignancy within the papilloma in 3 cases.

Papilloma of Rectum and Colon

In the K.C.H. series were 31 cases of papilloma of the rectum, 55% being in males whose average age was 56. The average age of the females was nearly 10 years older. The papilloma or villous tumour of the rectum is of two types, the sessile and the pedunculated. Each has a convoluted surface formed by villi closely packed together (Ewing 1950).

It has been customary to divide the simple epithelial tumours of the bowel into two distinct entities, the adenoma and the papilloma. Dukes (1947) first pointed out that the adenoma and the papilloma are not distinct and separate growths but variants of the same neoplasm. He suggested that the difference in form depends on where the most stimulation to the epithelium is received. If the stimulation is on the surface of the mucosa, the tumour will be villous because there is room for it to grow; but, if the stimulation is at the bottom of a crypt, the tumour will be pedunculated because space to grow is limited. Dukes has since suggested (1957) that the frond-like form of the papilloma of the bladder or bowel may be produced by the muscular contraction of the wall of the viscus forcing the tumour towards the centre of the lumen.

In the K.C.H. series 61% were single growths, 23% were multiple, and 16% encircled the bowel sufficiently to warrant a major resection. The theory of the multifocal origin of such tumours was supported in that in some cases from which a benign growth had been removed a second growth was found later in a position proximal to that of the first. Seeding as a method of spread was therefore unlikely.

As regards evidence that these growths are precancerous, only 3 of our 31 cases were associated with eventual malignancy, 2 of these are examples of where a papilloma which is clinically benign is removed, and, although histological examination shows it to be a carcinoma, there is no recurrence, simple removal being apparently adequate.

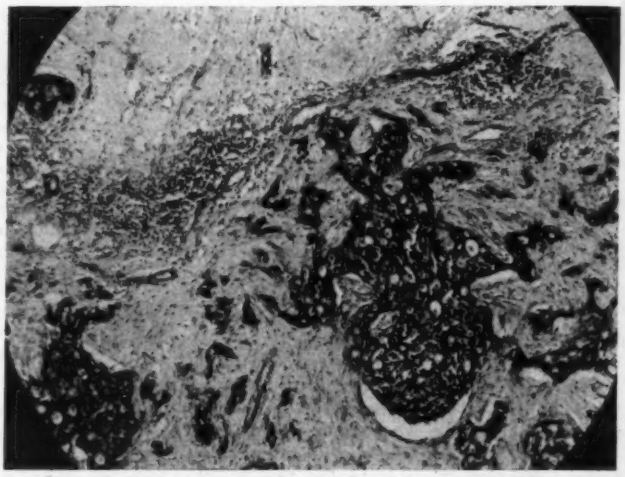

Fig. 2—Deeper portion of section shown in fig. 1. Note infiltration.

One of these cases was in a woman, of 63, from whom a papilloma was removed three times in three years. Two years after the last removal a fourth tumour was found at the same site and was also removed, but this time it was malignant and a major resection was carried out. Examination of the specimen showed that the removal of the initial growth had been complete, and there was no evidence of remaining malignant growth or metastases.

The second case was in a woman of 54 who had a number of rectal papillomata; some of these were benign, but others, whose appearance on sigmoidoscopy in no way differed from the rest, contained areas of carcinoma (Dukes' grade II) within the benign growth. As there was some doubt as to whether they were primary carcinomata or malignant change in a previously benign lesion, it was felt that the patient should be kept under observation after local removal of the tumours rather than be submitted to an abdominoperineal operation, which was the only alternative. Two years later there has been no recurrence.

The third case illustrates the opposite situation. A papilloma was removed from a woman of 62, but in the follow-up another growth was found which had not been present at the initial examination. Histological examination of two biopsy specimens showed a benign papilloma, but that of a third showed a poorly differentiated carcinoma. A major resection of the growth was done, and the operation specimen contained three growths. The most distal growth was a benign papilloma; above this was a sessile (Dukes' grade III) carcinoma; and the most proximal of the three was a pedunculated adenoma containing an area of well-differentiated carcinoma.

Sunderland and Binkley (1948) reported a series in which 68·7% of papillary adenomata showed areas of cytological carcinoma either in the original tumour or in a recurrence at the site of removal, but only 39·5% developed invasive properties. These workers point out that it is difficult to argue with those who maintain that those tumours which subsequently develop infiltrative properties must have been carcinomatous from the beginning, because it is impossible to make serial sections of these growths, and therefore no definite conclusion can be drawn. It would be unreasonable, however, to maintain

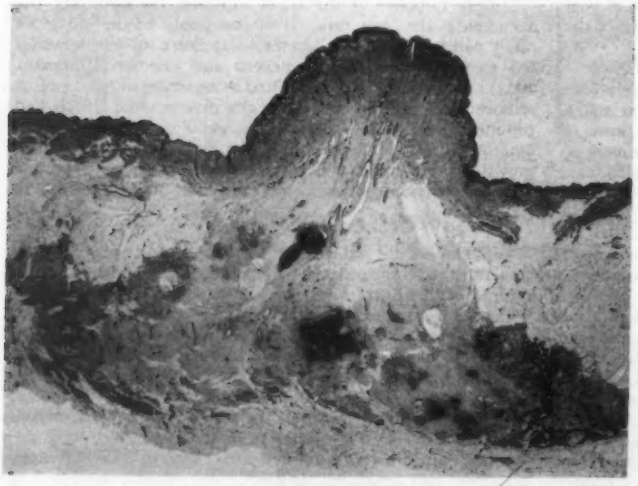

Fig. 1—Either two papillomata or the same papilloma in two areas immediately below nipple.

that a tumour which was a carcinoma from the beginning would recur superficially at irregular intervals and suddenly invade, metastasise, and cause death.

The disease known as familial intestinal polyposis is usually regarded as an entity, probably because of its striking mendelian characteristics rather than its pathology. Although the lesions are predominantly of the adenoma type, as Dukes (1952) states, they are another variety of the same neoplasm as is the papilloma, and papillomatous tumours are sometimes found side by side with the adenomata (Lockhart-Mummery et al. 1956). The incidence of malignant change in this condition is high, and cancer is most likely to be discovered about fifteen years after the first onset of the symptoms of polyposis—i.e., at about the age of 35. About 75% of patients with polyposis, if untreated, will develop cancer.

DUCT PAPILLOMA OF BREAST

As pointed out by one of us (Wakeley 1945, 1947), there is too great a tendency today to regard duct papilloma of the breast as malignant, or potentially malignant, and therefore requiring amputation of the breast. This idea shows a lack of thought, of experience, and of a thorough examination of every breast removed. Local amputation of the breast is an easy operation and it is wishful thinking to say that, because a young woman has a bloodstained discharge from the nipple, her breast should be removed because cancer might supervene. Of our 49 duct papillomata of the breast only 1 showed evidence of malignant change (figs. 1 and 2); and a bloodstained discharge from the nipple may be caused by carcinoma, by chronic cystic mastitis, or by papilloma.

Duct papillomata are nearly always found in the larger ducts and therefore are situated beneath or near the nipple or the areola. They can be excised through a radiating incision over the enlarged duct. Where an enlarged duct cannot be palpated, the nipple can be covered with collodion for two or three days, during which time the blood will accumulate in the duct and distend it, rendering it palpable.

Conservative surgery should be practised for duct papilloma of the breast, but a "follow-up" is necessary to prevent missing the odd case which might become malignant later.

CUTANEOUS PAPILLOMA

The papilloma of the skin has been defined as a tumour-like proliferation of the skin characterised by hyperkeratosis. According to this definition the following would be classified as papillomata: nævus verrucosus, the seborrhœic wart, senile keratosis, verruca vulgaris, and acanthosis nigricans. These conditions may appear similar in that they are papillary, but detailed dermatological and histological examination shows them to be distinct.

Nævus verrucosis may be single or multiple and is usually present at birth; it is benign. The *seborrhœic wart* or basal-cell papilloma is often mistaken for a malignant melanoma because of its colour, which varies from yellow to black; it, too, is benign. *Senile keratosis* occurs in the elderly, usually in patients over 60, the lesions being on the sites of exposure, commonly the face and the hands. About 20–25% of these growths are said to develop into squamous-cell carcinoma.

The two remaining clinical conditions are of more interest to the surgeon. *Verruca vulgaris* is the commonest example of a histological papilloma. It is believed to be caused by a virus, the lesion being commonest at the sites of trauma, especially the hands and knees, but it may occur in old operation scars. Virus-like particles have been obtained from some of these growths, which are distinguishable cytologically in that the cells contain eosinophil inclusion-bodies and vacuolated cytoplasmic masses (Bunting et al. 1952). The nuclear enlargement, distortion, and interference in the development of the epidermal cells probably reflect the effect of the virus.

Acanthosis nigricans occurs in two varieties, benign and malignant. The malignant is of surgical interest because, in half the cases occurring after middle age, the skin lesion, although benign, is associated with malignant disease elsewhere, usually in the alimentary tract, most commonly in the stomach (Curth 1943).

Of our K.C.H. series of 46 cases of cutaneous papillomata removed by surgery 34 (about three-quarters) were on sites of exposure, on either the face or hands. The combined average age was 59, the average age in the males being slightly less. 1 papilloma showed evidence of early malignant change.

Discussion

In attempting to assess the relationship of the benign papilloma to cancer we have sought for the common factors in the pathology and ætiology of papillomata in different parts of the body.

INCIDENCE AND SITE

With the exception of the virus papilloma, most papillomata in all sites occur in people over the age of 50. There is little difference in the incidence in the sexes except as regards the urinary tract, where the disease is predominantly in the male. In our series there was no papilloma of the bladder in women under the age of 50.

There may be a relationship between the sex hormones and acanthosis nigricans; Curth (1943) suggested that, in the benign type the skin lesion may be activated by one of the sex hormones, for the benign lesion is usually found in a young patient and appears at puberty, or, if already present, tends to spread at this time.

If the papilloma is caused by some stimulant, one would expect the growths to be most common at sites of exposure. This is probably true of growths on the skin (three-quarters were on sites of exposure) and the bladder, and to a lesser extent for those in the alimentary tract, except perhaps the rectum. In the mouth the growths are commonest on the pillars of the fauces and on the soft palate, which are perhaps the sites most easily affected by trauma and a stimulant. The adenopapilloma of the alimentary tract is most often found in the rectum, and it is possible that, here again, the stimulant has the greatest opportunity of access, because not only are the fæces harder and more traumatic at this point but stagnation is greater here than in the upper reaches of the bowel. In the bladder the papilloma is most common near the ureteric orifices. There is some similarity in the figures from clinical and experimental sources: in 67% of cases in the series the growths were near the ureteric orifices, and in animals in which bladder tumours were artificially induced by feeding with B-naphthylamine 30% of the growths were on the lateral walls and 33% on the posterior wall of the bladder (McDonald and Lund 1954). Kaplan et al. (1951) have pointed out that lesions which involve the ureter are most often found at the anatomical points of narrowing.

PATHOLOGY AND PATHOGENESIS

From the work of Dukes (1947, 1952) and Willis (1953) it is evident that the adenoma and the villous papilloma of the stomach, intestine, and rectum are not separate tumours but variations of one neoplasm. In considering how these tumours are formed and what relation they bear to cancer three questions arise:

(1) *Is the Papilloma Precancerous and, if so, is it Malignant Initially?*

Clinical and experimental work shows that the papilloma is a potential source of cancer. Clinically it is difficult to determine which of these growths will become malignant, and sometimes it seems that, in the long run,

the clinical assessment of malignancy may prove more accurate than the histological examination. One can only repeat what has been said before: some of these benign growths will remain benign, some will become malignant soon, and some will have malignancy thrust upon them. In some tissues a papilloma tends to become malignant rapidly, and one suggestion is that such tumours do not undergo transition from a benign to a malignant state but have concealed malignancy from the beginning of their growth. This may be true of some but not every such tumour, because there is ample evidence that malignancy may develop in a lesion which has been benign for many years, and some benign neoplasms contain a focus of carcinoma which is not invasive. Macalpine (1947) supported the teaching of Dukes: a urinary papilloma may be benign in one part and malignant in another, and a papilloma may be malignant but not necessarily invasive.

(2) *How do Multiple or Successive Growths Arise?*

Benign and malignant lesions may arise side by side, suggesting that the whole area contains foci of potential

Fig. 3—Transitional-cell papilloma of bladder.

tumours. Experimental work on the bladder and the gallbladder shows the same thing.

Bonser and Jull (1956) implanted a chemical carcinogen into the bladders of mice for about a third of their life-span and produced a variety of epithelial change varying from hyperplasia to frank carcinoma. So the question whether carcinoma is preceded by a graded series of epithelial changes or not was again raised by these experiments. These workers conclude that, although some cancers arise in benign lesions, others appear to arise spontaneously, but in nearly all the bladders there was evidence of epithelial hyperplasia. Though many bladders contained only a single tumour, there was adequate evidence of the multifocal origin of cancer.

Similar results were obtained in cats' gallbladders in which carcinoma had been induced by implanting within the gallbladder a single pellet of methylcholanthrene (Fortner 1955). Papillomata were found together with carcinoma; and, although the carcinogen was applied to the entire surface of the gallbladder, malignant change did not take place uniformly, and benign epithelium was seen adjacent to malignant.

Although there is evidence that multiple growths may arise from multifocal areas of neoplastic change, this is not the only method of growth; spread may still take place by transplantation and implantation. Exfoliated

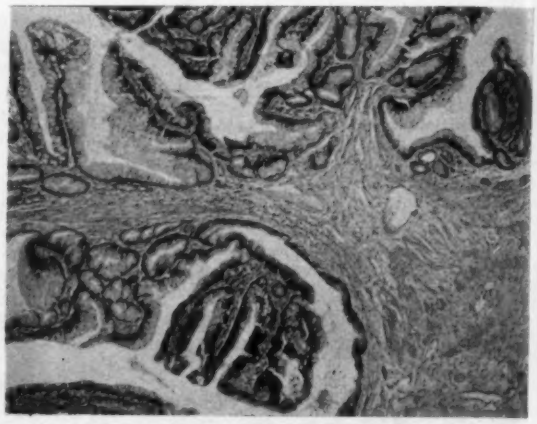

Fig. 4—Benign adenoma of rectum.

cells from tumours of the bowel may become implanted on the suture line of an anastomosis, and cells from a papilloma of the urinary tract become implanted in the wounds and sites of instrumental trauma. Experiments have also shown that exfoliated growths can become implanted in intact bladder epithelium where there is stagnation of urine.

McDonald and Thorson (1956) made "Pavlov pouches" in the bladders of dogs in which there would be stagnant urine and placed in them loose fragments of papillary growths induced in other dogs fed with β-naphthylamine. In 3 of 7 dogs the growth became implanted in the intact bladder epithelium. These papillary tumours resembled their progenitors microscopically and were regarded as papillary carcinomata.

Marcus (1953) described a case in which stagnation of urine may possibly have played a part. The patient had a scrotal cystocele in an inguinal hernia which had been present for twenty-five years. The cystocele contained three benign papillomata, but there was none in the remainder of the bladder.

(3) *How is the Tumour Initiated?*

Clinical and experimental evidence shows that an area of tissue may undergo neoplastic change varying from hyperplasia to invasive malignancy. The variety of these epithelial changes postulates that the stimulation which produces them must vary either in kind or in degree.

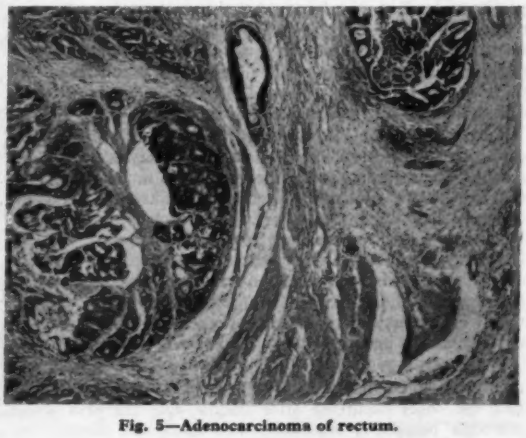

Fig. 5—Adenocarcinoma of rectum.

In the skin the change may be produced by a virus in adolescence, but the growths of the elderly suggest that the stimulant may take a considerable time to produce its effect. This may also be true for the papillomata of the alimentary and urinary tracts. Experimental tumours have been produced in the urinary tract by chemical stimulation. This raises the question whether similar stimulation may take place in the bowel by breakdown products of bile or of food.

Boyland et al. (1955) found a high level of glycuronidase in patients with bladder growths and in patients who, as the result of treatment, were clinically free from growth. They suggest that an enzyme present in unusual abundance may liberate a carcinogen from the urine.

Holsti and Ermala (1955) painted with tobacco tar the lips and mouth of mice to study its effect on the oral mucosa. No local change was produced, but 52 of 60 mice had papillomata in the bladder, mainly near the trigone. In 6 mice malignant change had occurred at the base of the papilloma. The control mice developed no tumours; nor did this strain exhibit tumours spontaneously.

Further evidence has been produced that substances which stimulate tumour formation are excreted in the urine:

McDonald and Lund (1954) made "Pavlov pouches" in the bladders of dogs so that the mucosa of the pouches was excluded from contact with urine. The dogs were then fed with β-naphthylamine. Papillary growths of transitional carcinoma developed only in those portions of the bladder which were in contact with urine.

A man, aged 69, with gross papillomatosis of the bladder underwent total cystectomy and transplantation of ureters in 1953 (Parker 1957). Three years later he was found to have a papillomatous growth in the bowel below the level of the ureteric openings. The operation specimen contained two growths, a poorly differentiated adenocarcinoma and a benign rectal papilloma (figs. 3–5).

Although neoplastic change in all its phases can be produced by direct chemical stimulation, this process may be complicated in that more than one stimulus may be involved.

Urethane was painted on the skin of mice, but no tumours were produced; repeated applications of croton oil alone produced very few tumours; but the application of urethane followed by repeated applications of croton oil (Salaman and Roe 1953, Roe and Salaman 1954) gave rise to many epidermal tumours, some of which were malignant. The number of tumours which arose was proportional to the dose of urethane applied. The results of this experiment suggest that there may exist "incomplete carcinogens"; in this case urethane acted as an "initiator" and croton oil as a "promoter".

Selbie and Robinson (1947) showed that the yields of papillomata produced by the transmissible Shope virus on rabbit's skin when the skin was pretreated with croton oil before the inoculation of the virus were much greater than those obtained on untreated skin. Selbie and Robinson (1948) also showed that carcinomatous transformation occurred regularly in this transmissible papillomatosis, especially in rabbits bearing papillomata for twelve months or more. There was a higher incidence of carcinomatous change in papillomata arising from skin which had been treated with croton oil before inoculation.

Selbie and Robinson (1947, 1948) state that, although carcinomatous transformation appears to be a natural stage in the development of this virus infection, it presents such a radical alteration in behaviour that it is difficult to see how this could be a continuous process, because indolent papillomata which have remained quiescent for long periods suddenly begin to grow rapidly and become malignant.

Summary

The papilloma at any site is a potential source of cancer, although it is least so in the skin.

The multiplicity and coexistence of papilloma and carcinoma is probably due to multifocal neoplastic change in an area of tissue, and different phases of this change, varying from papilloma to malignancy, both without and with invasion, may be present either simultaneously or at different times.

The stimulus to the dividing cell may be produced by direct chemical stimulation, or by a virus attack, which itself is probably a disturber of cellular biochemistry or by a simple mutation.

We are grateful to Mr. Geoffrey Parker, Mr. E. G. Muir, and Mr. J. G. Yates-Bell for permission to include their cases in this report. We wish to thank Dr. Cuthbert Dukes for his kindly advice, and Dr. Stretton Young and Dr. M. E. Powell for the photomicrographs.

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"... Medicine is at heart a polygamist becoming wedded to as many of the sciences and practical arts as prove their worth. Nor has medicine lacked for would-be mates, the most recent and vocal of these being the psychological and social sciences. If these have at times seemed importunate and impatient, this may be because they feel themselves to have been left, for too long, to cool their heels in the vestibule. And if at other times, they have acted shy and perhaps overly diffident, this may be because it is a source of wonder to them that they are being considered at all. Moreover, as is often the case with polygamy, the first set of wives—say, the biological and chemical sciences—are reluctant at first to approve yet another burden to the ménage. But there is still hope. As the burden of work plainly becomes more than can be managed by the present members of the household, they become ready for new accessions to help carry the load of what needs to be done."—R. K. MERTON, *The Student-Physician*; p. 32. Cambridge, Mass., 1957.

ESSENTIAL FATTY ACIDS, LIPID METABOLISM, AND ATHEROSCLEROSIS *

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WORK done in this laboratory in 1950–52 showed that the ingestion of certain different vegetable fats, under precisely controlled conditions, was associated with a major sustained fall in the level of plasma-cholesterol and plasma-phospholipids (Kinsell et al. 1952, 1953). This work has been confirmed by Ahrens et al. (1955), Beveridge et al. (1955, 1956), Malmros and Wigand (1955, 1957), Bronte-Stewart et al. (1956) and others. Clinical observations of Groen et al. (1952) and Groen (1957) also have indicated significant differences between the effects of fats of animal and vegetable origin as regards plasma-cholesterol levels, possibly in relation to some of the manifestations of atherosclerosis.

Our studies in 1951–55 indicate (by exclusion and by direct evidence) that the polyunsaturated fatty acids in the diet are the common factor probably responsible for these effects on plasma-lipids (Kinsell and Michaels 1955, Friskey et al. 1955, Kinsell et al. 1956a and b); but the following questions remain to be answered:

(1) Do polyunsaturated fatty acids per se lower the plasma-cholesterol level as efficiently as do natural fats containing the same amounts of the same acids?

(2) Is linoleic acid an essential fatty acid in man, as it is in the rat? If so, are characteristic plasma-lipid patterns associated with a deficiency and an abundance of this acid in the diet?

(3) Is anything known about the way in which essential fatty acids lower the plasma-cholesterol level?

(4) Are the changes in plasma-lipid levels associated with the ingestion of fats containing linoleic acid desirable because they either prevent or improve atherosclerosis?

(5) If so, can the desired change in the plasma-lipid levels be achieved by "fortification" of mixed diets, especially those containing customary amounts of animal and dairy fats?

(6) Are diets containing large amounts of essential fatty acids better or worse than diets containing very little fat in lowering the plasma-lipid levels to prevent or to improve atherosclerosis?

(7) Are more unsaturated fatty acids than linoleic acid (e.g., arachidonic acid) more effective than it in lowering the plasma-cholesterol level?

On the basis of data accumulated in this laboratory over the past three years partial or complete answers to the above questions are available.

* Presented in part at the Gordon Conference on Lipids (June, 1957), the Fourth International Conference on Lipids (Oxford University, July, 1957), and the International Congress on Nutrition (Paris, July, 1957). This work has been supported in part by grants from the Schering Corporation, the Armour Laboratories, the Borden Company, the Upjohn Company, the Alameda County Heart Association, and the National Institute of Health. Grateful acknowledgment is made to members of the research staffs of the Armour Laboratories, the Pacific Vegetable Oil Company, and Procter and Gamble for supplies of lipid materials used in these studies; to Merck and Company for supplies of digitonin; to the Borden Company for supplies of 'Borden Instant Coffee'; to the Nestle Company, Inc. for 'Nestea'; and to Mead Johnson and Company for 'Casec' used in the balance studies.

Methods

Unless otherwise indicated, all the studies reported were made in patients in the metabolic ward. Nutrients were provided as homogenised mixtures and consumed hourly from 9 A.M. to 9 P.M. These formulæ were chemically constant in a precise quantitative sense and were nutritionally adequate in terms of calorie content and quantity and quality of proteins, minerals, and vitamins (including generous amounts of crude desiccated liver). Unless otherwise indicated, the only variables were fat and carbohydrate.

The methods of determining most of the lipids have been described previously (Kinsell et al. 1953). The quantitative chromatographic separation of plasma-cholesterol esters and the colorimetric determination of iodine values were done by the method of Michaels et al. (1958).

Determinations of substances in stools and urine were done on portions of seven-day specimens.

Experimental and Clinical Observations

(1) *Do polyunsaturated fatty acids per se lower the plasma-cholesterol level as efficiently as do natural fats containing the same amounts of the same acids?*

Case 1—Table I shows the findings in a man, aged 27, with familial hypercholesteræmia. Between the ages of 22 and 26 he had two episodes of myocardial infarction. Before admission to the metabolic ward he received amounts of safflower oil which, in more than 90% of patients studied, produced and maintained a profound fall in the plasma-cholesterol level. In this patient, however, the plasma-cholesterol level did not fall (compared with values on a low-fat regimen); but the iodine value of his plasma-cholesterol fatty acids increased from less than 100 to more than 140.

Treatment and progress.—On admission to the metabolic ward he received initially a chemically constant and fat-free diet followed by the substitution, for calorically equivalent amounts of carbohydrate, of 40, 60, and finally 80 g. of purified ethyl linoleate. Consumption of the fat-free diet was associated with a fall in the plasma-cholesterol level and a decrease in

TABLE I—FINDINGS IN CASE 1 WITH FAMILIAL HYPERCHOLESTERÆMIA

Date	Diet	Plasma-cholesterol level (mg. per 100 ml.)	Cholesterol-ester-fatty-acid iodine value	Plasma-neutral-fat (mg. per 100 ml.)	Plasma-phospholipid level (mg. per 100 ml.)	Fecal sterols (g. daily)	Fecal fat (g. daily)
March 25	2000-cal. fat-free	375	158	496	334		
28		391	136	qns	310		
April 1		350	117	449	284		
4		347	135	375	270	0·72	0·9
6		326	114	331	255		
8	2000-cal. with ethyl linoleate 40 g.	326	138	343	250		
10		307	138	344	256		
11		306	150	261	290	1·23	0·6
13		366	172	261	295		
15		341	167	291	273		
17		340	151	339	275	1·35	1·2
18		313	156	315	247		
22	2350-cal. with ethyl linoleate 40 g.	315	185	291	270		
24		317	158	296	273	1·20	1·0
25		325	154	258	273		
29	2450-cal. with ethyl linoleate 60 g.	273	156	317	241		
May 1		300	162	297	247	1·56	1·3
2		298	155	280	255		
5		323	154	358	254		
6		306	150	271	245	1·16	0·8
8		300	156	275	247		
9		269	156	231	220		
13		262	167	373	247		
15		295	142	360	270	1·41	0·6
18		296	152	348	263		
20	2750-cal. with ethyl linoleate 80 g.	300	154	302	243		
22		255	139	298	268		
23		267	145	303	313	1·23	1·1
25		331	164	146	357		
26		293	139	242	257		
27		291	150	259	268		

the cholesterol-ester-fatty-acid iodine value. The addition of ethyl linoleate to the diet was associated with a further fall in the plasma-cholesterol level and an immediate increase in the cholesterol-ester-fatty-acid iodine value.

It can be concluded from the evidence presented in this patient and in a healthy boy (table II) that question 1 is answered in the affirmative.

(2) *Is linoleic acid an "essential" fatty acid in man, as it is in the rat? If so, are characteristic plasma-lipid patterns associated with a deficiency and an abundance of this acid in the diet?*

Table II shows the findings in case 2, a healthy boy, aged 19, who was in hospital with a fractured femur. It is apparent that, compared with the fat-free diet, the addition of ethyl linoleate to the diet produced a profound fall in the fasting plasma-cholesterol, neutral-fat, and phospholipid levels and an increase in net unsaturation of cholesterol-ester-fatty acids to values well in excess of the administered material. When oleate was substituted for linoleate, the plasma-cholesterol, neutral-fat, and phospholipid levels slowly rose after an initial "lag period", and the iodine value decreased rapidly. The "lag period" associated with the initial administration of oleic acid was probably related to the availability of essential fatty acids from depots as the result of previous administration of linoleate as well as to contamination of the oleate with linoleate and linolenate (1–6% in different preparations).

These results in this healthy boy supply affirmative answers to the questions raised in item 2. Further studies will be required to substantiate this conclusion and are under way.

We cannot explain the increased fæcal excretion of sterols noted during feeding with oleate. No such effect was noted in case 6 (table v). Additional studies now in progress may clarify this finding. Other linoleate data are contained in table v.

TABLE II—FINDINGS IN A HEALTHY BOY AGED 19

Date	Diet	Plasma-cholesterol level (mg. per 100 ml.)	Cholesterol-ester-fatty-acid iodine value	Plasma-neutral fat (mg. per 100 ml.)	Plasma-phospholipid level (mg. per 100 ml.)	Fecal sterols (g. daily)	Fecal fat (g. daily)
May							
16	2500-cal. fat-free	153	158	219	181		
17		166	166	196	178		
18		171	131	212	210		
19		160	122	229	189		
20		150	149	274	189		
22		118	150	262	178	0·76	1·1
23		105	147	365	211		
27		140	148	535	258		
29		135	141	405	220		
30		132	135	398	206	0·37	0·9
June							
3		141	120	426	215		
5		150	117	351	208	1·01	0·8
6		145	108	338	218		
10	Ethyl linoleate	148	118	375	213		
12	80 g. added	148	201	229	188	0·62	7·1
13		105	211	180	183		
17		90	180	219	131		
19		76	175	267	122		
20		78	259	202	103	0·67	2·7
22		88	275	219	140		
24	Ethyl oleate	95	248	217	125		
26	80 g. added	100	159	201	138		
27		78	173	233	125	1·43	3·1
29		79	163	232	161		
July							
1		103	108	317	156		
3		115	168	347	163		
4		117	164	337	188	1·87	1·9
5		115	167	265	167		
8		133	135	322	181		
10		130	135	302	181		
11		117	143	303	188		
15		122	144	282	200	1·60	0·79
17		126	152	281	169		
18		123	158	236	181		

TABLE III—FINDINGS IN CASE 4

Date	Diet	Plasma-cholesterol level (mg. per 100 ml.)	Cholesterol-ester-fatty-acid iodine value	Plasma-neutral fat (mg. per 100 ml.)	Plasma-phospholipid level (mg. per 100 ml.)	Fecal sterols (g. daily)	Fecal fat (g. daily)
Jan.							
21	2000-cal. with	165	131	148	187		
23	200 g. lard	140	—	181	160	—	10·0
25		145	—	186	168		
28		175	109	147	206		
Feb.							
1		173	—	160	194	—	6·8
4		163	143	201	166		
8		156	99	216	178	0·95	12·88
11	150 g. lard,	159	109	228	175	0·78	8·59
15	50 g. safflower	151	—	218	175		
18	oil	148	127	235	181	0·61	9·09
22		164	—	269	175		
25		179	—	199	170		
28		168	—	160	169	0·71	8·4
March							
1		178	—	159	168		
4	100 g. lard,	184	144	164	181		
8	100 g. safflower	140	—	228	160	0·74	8·8
11	oil	150	148	177	160		
15		158	—	179	160	0·36	9·6
18		140	—	203	153		
21		134	—	235	153	0·91	10·2
25		135	136	232	169		
28		125	185	211	150	1·15	21·1
April							
1	50 g. lard,	113	179	—	—	1·01	15·6
4	150 g. safflower	130	130	220	144		
8	oil	132	—	227	140	1·47	13·2
11		145	—	173	175		
15		154	199	203	156	2·07	16·9
18		153	150	233	162		
22	200 g. safflower	147	187	250	162	1·11	7·4
25	oil	149	—	213	172		
29		128	166	232	163		

(3) *Is anything known about the way in which essential fatty acids lower the plasma-cholesterol level?*

No. A working hypothesis which is not incompatible with available data and which is susceptible to systematic experimental assessment is considered below.

(4) *Are the changes in plasma-lipid levels associated with the ingestion of fats containing linoleic acid desirable because they either prevent or improve atherosclerosis?*

No answer which applies with certainty to the population at large is available, nor will it be for some time. On the basis of certain observations, however, a provisional answer may be at hand. In the past three years more than 80 outpatients with known vascular disease were observed before and during the consumption of diets containing large amounts of fats rich in linoleic acid.

The fats used included cotton-seed, soy, corn, walnut, peanut, and safflower oil. At present safflower oil is being used almost exclusively because it contains more linoleic acid than does any other fat which is readily available commercially (70–80% in most lots). According to the caloric requirement and clinical status of the patient 40–180 g. daily of such fats was included in the diet. The precise make-up of these diets is being reported by Olson and Kinsell (1957).

Many of the same problems which apply to the management of diabetics apply to dietary regulation of this group of patients. None of these problems is insurmountable. For any patient to be admitted to a semi-controlled clinical programme designed to provide interpretable answers, certain basic requirements are necessary in the patient: integrity, adequate intelligence, and willing cooperation. There must be adequate personnel and facilities for group and individual instruction, periodic clinical assessment, dietary supervision, and precise laboratory follow-up.

Patients observed in the ambulatory group included those who had had one or more coronary occlusions, those with cerebral vascular disease, those with various forms of xanthomatosis, and those aged less than 50 with peripheral vascular disease.

The only statement we are prepared to make about the coronary group (more than 50 patients, some of whom have been followed up more than three years) is that all the patients "feel better" who have kept to the diet rich in essential fatty acids and no patient has had a new coronary occlusion while taking a diet rich in vegetable fat. Most of these patients had been on a low-fat diet before the study. In view of the opinion prevailing in most quarters before 1956 that "fats were bad" regardless of the nature of the fat, we had some trepidation about giving these patients high-fat diets. Hence the absence of clinical evidence of progressing disease has been gratifying. If such freedom from new coronary occlusion continues for a significant time one may be entitled to draw conclusions, but hitherto the study has been too short and the patients have been too few.

Several of the patients with cerebral vascular insufficiency feel better on a diet rich in essential fatty acids, but there is no adequate way of assessing this statement at present.

As regards the patients with peripheral vascular disease, we have reason to believe that something desirable has happened in association with the high intake of essential fatty acids; but oscillometric readings are notoriously unreliable, and it is well recognised that relative vascular insufficiency in the legs fluctuates as regards functional capacity. However, when functional improvement is consistently associated with a specific programme, there may be reason to believe that it is more than coincidental.

Case 3—A man, aged 47, was referred for assessment in September, 1956, with severe pain and cramping in his legs, and angina pectoris on slight exertion. He had had two myocardial infarctions. His weight was normal for his height and age and has remained so. Pulsation was absent bilaterally from his dorsalis pedis and posterior tibial arteries.

Treatment and Progress.—On Sept. 20, 1956, he was changed from the low-fat 1800-calorie diet which he had taken for a long time, with progressive deterioration of his clinical status, to an 1800-calorie diet containing about 135 g. of cottonseed or of safflower oil daily (Olson and Kinsell 1957). On this he continued until March 2, 1957. By Oct. 18 walking was less of an effort, but he still had much angina. By Jan. 10, 1957, he could "walk indefinitely" (compared with the length of three city blocks in October, 1956). On Feb. 2, he stated that he had walked twenty blocks without effort, and that he was free from chest pain. On March 2 he had returned to the full activity as a "trouble-shooter" for the telephone company (after two and a half years' disability sufficient to prevent him from participating in anything except office work). On this date he was changed to an 1800-calorie diet containing about 70 g. of fat including more than 35 g. of linoleic acid. In mid-April questionable pulsations were felt in his right posterior tibial artery. On June 22 pulsations were strongly palpable in both posterior tibial arteries, and questionable pulsation was noted in his right dorsalis pedis artery.

TABLE IV—FINDINGS IN CASE 3

Date	Diet	Plasma cholesterol level (mg. per 100 ml.)	Plasma-neutral-fat level (mg. per 100 ml.)	Plasma-phospho-lipid level (mg. per 100 ml.)
Oct. 19	1600-cal.	170	317	209
,, 21	100 g. coconut oil	183	173	202
,, 24		200	108	203
,, 26		164	221	195
,, 28		165	316	206
,, 31		154	233	213
Nov. 2		183	209	213
,, 4		172	335	194
,, 7		163	172	181
,, 9	80 g. coconut oil	173	155	203
,, 11	20 g. soy	178	156	195
,, 14		169	198	213
,, 16		179	—	218
,, 18		170	—	181
,, 21		173	—	188
,, 23		175	—	191
,, 25		151	—	188
,, 28	50 g. coconut oil	150	—	183
,, 30	50 g. soy	143	166	175
Dec. 2		143	165	156
,, 5		125	195	156
,, 7		117	214	154
,, 9	20 g. coconut oil	103	167	144
,, 12	80 g. soy	94	166	125
,, 14	100 g. coconut oil	109	294	147
,, 16		109	325	169
,, 19		136	—	—
,, 21		161	213	172
,, 23		174	145	180

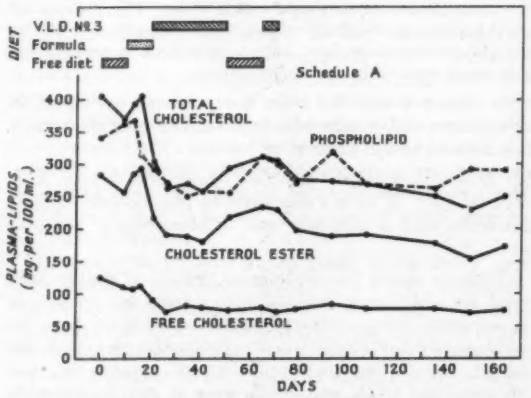

Fig. 1—Semi-controlled study in an ambulant patient. The formula and Schedule A diets and vegetable lipid diet no. 3 all contained more than 35 g. of linoleic acid daily and little animal fat. These diets are described by Olson and Kinsell (1957).

Of the other patients with peripheral vascular disease several have shown equally good symptomatic and functional improvement. None has yet shown return of palpable pulsation in vessels in which, before the diet rich in essential fatty acid, no pulsation was felt.

All of those who have responded have shown the usual considerable sustained fall in plasma-cholesterol level. In some this has been associated with a decrease in the cholesterol/phospholipid ratio. Studies of fatty-acid composition of the plasma-cholesterol esters have not been possible until recently in this group.

All this is consistent with an affirmative answer to question 4. Further observation is obviously required.

(5) *If the answer to question* 4 *is in the affirmative, can the desired change in the plasma-lipid levels be achieved by "fortification" of mixed diets, especially those containing customary amounts of animal and dairy fats?*

It may be well to consider certain precisely controlled metabolic studies in which mixtures of vegetable and animal fat are used. Table III illustrates such a study.

Case 4—A man with mild diabetes received a chemically constant diet containing 200 g. of fat daily. He was free from demonstrable vascular disease and had a low plasma-cholesterol level on any diet given him. When lard comprised the only source of fat, or when 50 g. of safflower oil was substituted for an equal amount of lard, the cholesterol levels remained practically constant. The safflower oil used in this study contained 73% of linoleic acid. Increase of the safflower oil to 100 g. instead of an equal amount of lard led to a prompt and major fall in the plasma-cholesterol level. The averages

for cholesterol-ester-fatty-acid iodine values were significantly greater during this period.

Table IV shows the finding in a woman aged 49, with no evidence of vascular disease, in whom coconut oil was " titrated " against soya oil. As with lard and safflower oil, a 50% substitution of soy for coconut was required to obtain a major fall in plasma-cholesterol level. The coconut oil contained practically 100% saturated acids, and the soy oil contained about 50% linoleic acid and some linolenic acid.

Fig. 1 shows the findings in an ambulant male outpatient, aged 58, with hypercholesterolæmia, xanthelasma, and clinical evidence compatible with probable generalised asymptomatic atherosclerosis. During the course of formula and mixed diets, which contained two or more parts of highly unsaturated fat to one portion of predominately saturated fat, a very significant and maintained fall in the plasma-cholesterol level was observed in this extremely cooperative patient.

Observations during the last four years indicate that young healthy adults require a quite small proportion of linoleic acid to the sum of saturated fatty acid and fatty-acid precursor to maintain a relatively low plasma-cholesterol level. The greater the amount of vascular disease, the larger is the amount of essential fatty acids required to lower the plasma-cholesterol level. It seems not unreasonable to relate this observation to impairment of efficiency to conserve and/or utilise essential fatty acid in the abnormal individuals. Whatever the reasons, it seems probable that 10 g. of linoleic acid in a young healthy person is sufficient to keep the plasma cholesterol and phospholipid levels below 170 mg. per 100 ml., if the dietary intake is otherwise " average ". Very abnormal patients—e.g., some with xanthomatosis—may require more than 50 g. of linoleate daily in association with a relatively low intake of saturated fatty acid and precursor thereof.

Approximate requirements in three groups are shown diagrammatically in fig. 2. In patients with known vascular disease who initially respond poorly to the mixed diet, it is our custom to limit the intake of food to a formula diet plus supplemental vitamins for one to four months, or until the cholesterol level has reached and been maintained at a normal level for more than a month. The greater efficiency of the mixed diet after such " loading " may be referable to relatively high concentration of polyunsaturated fatty acids in the fat depots as well as to possible improvement in the efficiency of conservation and utilisation of essential fatty acids.

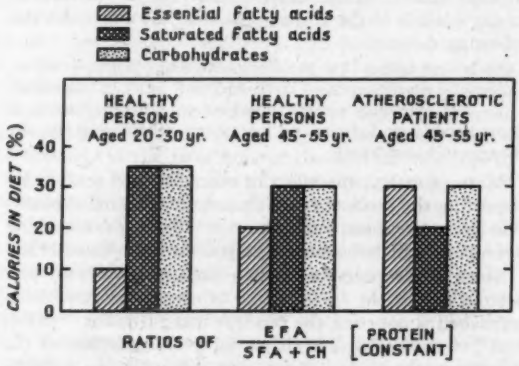

Fig. 2—Approximate requirements of essential fatty acids in relation to age and pathology. This is a rough approximation subject to later correction. The diets used in the studies on which these approximations are based contained more than average amounts of protein.

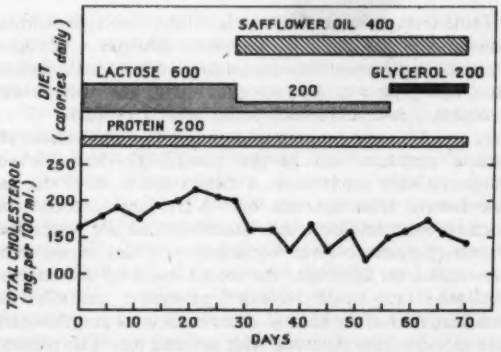

Fig. 3—On fat-free 800-cal. diet plasma-cholesterol level rose. Substitution of 44 g. of ethyl esters of safflower fatty acids for calorically equivalent amount of carbohydrate was associated with progressive fall of the plasma-cholesterol level. Patient was in nitrogen equilibrium throughout.

To summarise, it appears that the inclusion of adequate amounts of natural fats containing 40–80% of linoleic acid in mixed diets will lower the plasma lipid levels. The actual amount of linoleic acid required depends on the composition of the diet and the clinical status of the patient.

(6) *Are diets containing large amounts of essential fatty acids better or worse than diets containing very little fat in lowering the plasma-lipid levels to prevent or to improve atherosclerosis?*

For the reasons noted above it is extremely difficult to assess the clinical efficacy of any diet. Our only comment would be that all the patients with partially occlusive vascular disease who improved clinically on a diet containing plenty of linoleic acid had for a long time been taking diets containing extremely little fat. On these diets, in the opinion of the patients and their physicians, their course had been progressively downhill.

As regards the virtues of a low-fat diet in terms of plasma-cholesterol level, the answer is very much more easily obtained. A low-fat diet is, of necessity, a high-carbohydrate diet. Fig. 3 shows a portion of a study in an obese female with no evidence of vascular disease. While she was receiving a fat-free low-calorie diet the plasma-cholesterol level rose progressively. When 100 g. of carbohydrate was replaced by a calorically equivalent quantity of the ethyl esters of fatty acids derived from safflower oil, there was a highly significant fall in the plasma-cholesterol level and this was maintained.

The findings in a healthy control (table II) also emphasise the remarkable qualitative and quantitative differences in the plasma lipids during the intake of a " no-fat diet ", compared with a dietary including large amounts of essential fatty acids.

From these studies it appears that diets rich in essential fatty acids are much more effective in lowering plasma-lipid levels than are very low-fat (high-carbohydrate) diets. Time and further work will provide additional information on the relationship of such diets to atherogenesis.

(7) *Are more unsaturated fatty acids than linoleic acid (e.g., arachidonic acid) more effective than it in lowering the plasma-cholesterol level?*

An approach to an answer to this question has been most difficult because of the unavailability of purified arachidonic-acid preparations.

Table v shows some findings in a hypercholesterolæmic patient with xanthomatosis and mild diabetes. Administration of a phosphatide mixture derived from mammalian liver, with a fatty-acid composition of 12·5% of tetranoic (probably cis-arachidonic) acid, saturated acids 75%, oleic acid 5%, and conjugated dienes 2·4%, was associated with a profound fall in the plasma-cholesterol level, compared with the level on a diet in which all of the fat was derived from coconut oil. Very large amounts of purified ethyl linoleate and trilinolein did not lower the plasma-cholesterol level so much. When oleate was substituted for linoleate, the iodine value of the cholesterol-ester fatty acids decreased promptly; and after an initial lag period the plasma-cholesterol level progressively rose to the values observed with coconut oil. The reasons for the lag period are probably identical with those noted in the healthy young male (table II).

This study is compatible with the concept that arachidonic acid may be a much more potent hypocholesterolæmic agent than linoleic acid (see below).

TABLE V—FINDINGS IN PATIENT WITH XANTHELASMA AND DIABETES

Date	Diet	Plasma-cholesterol level (mg. per 100 ml.)	Cholesterol-ester-fatty-acid iodine value	Plasma-neutral fat (mg. per 100 ml.)	Plasma-phospholipid level (mg. per 100 ml.)	Faecal sterols (g. daily)	Faecal fat (g. daily)
March							
11	1850-cal. 75 g. coconut oil	311	—	246	320	0·58	3·2
15		313	—	362	316		
18		288	129	341	310	0·49	2·2
21		330	—	372	347		
25		276	118	qns	313	0·19	1·9
28		313	—	428	306		
April							
1	75 g. arachido-phosphatides	318	126	367	328		
4		240	156	329	260	2·12	13·4
6		235	194	302	257		
8		234	153	318	260		
10		210	150	358	282		
11		206	164	304	257	2·72	14·4
13		240	170	249	281		
15		240	154	277	263		
17		233	178	340	265	2·16	11·4
18		235	176	293	269		
22	37·5 g. arachido-phosphatides, 37·5 g. coconut oil	240	184	309	256		
25		273	183	285	280	1·92	9·7
29		242	194	318	278		
May							
1		255	186	347	300	2·04	11·9
2		267	—	349	294		
6	37·5 g. coconut oil, 37·5 g. ethyl linoleate	305	171	305	306		
8		283	173	314	283	0·54	1·3
9		257	173	226	263		
13		270	—	260	269		
15		287	159	331	300	0·52	1·1
16		262	150	282	343		
20	25 g. coconut oil, 50 g. ethyl linoleate	319	142	303	288		
22		270	154	349	323	0·65	2·4
23		270	144	268	285		
27	25 g. coconut oil, 50 g. trilinolein	260	130	286	285		
29		265	146	287	269		
30		265	156	264	256	0·43	1·1
June							
3		281	150	273	256		
5	75 g. trilinolein	280	169	345	300		
6		301	173	229	298		
8		263	197	257	281	0·83	1·5
10		260	184	268	255		
12		270	181	220	258		
13	75 g. triolein	260	184	241	255		
15		252	170	320	256	0·41	1·6
17		232	170	300	268		
19		237	142	338	275		
20		235	128	320	258		
24		240	125	315	269	0·56	0·8
26		235	119	213	263		
27	75 g. ethyl oleate	258	135	347	267		
29		247	109	334	288		
July							
1		253	134	284	294		
3		253	129	371	356		
4		266	130	346	300	0·97	1·3
5		280	118	368	302		
8		275	138	327	269		
10		305	126	339	295		
11		300	122	313	319	0·56	2·75
15		293	132	372	317		
17		322	qns	qns	288		
18		297	143	165	285		

Discussion

There appears to be no question but that a high intake of polyunsaturated fatty acid can produce a major fall in plasma-cholesterol level and a net increase in unsaturation of the cholesterol-ester-fatty acids. Comparable qualitative and quantitative changes in the plasma-lipids do not result from the intake of a low-fat or a fat-free diet, from a diet containing oleic acid as a source of unsaturated fatty acid, or under any other conditions of which we are aware. This by no means excludes the concept that factors in vegetable fats other than the polyunsaturated fatty acids have some significant effect on plasma-cholesterol levels. Beveridge et al. (1955, 1956) have excellent evidence that the addition of β-sitosterol to a low-fat diet will lower the plasma-cholesterol level. They feel that there is possibly some synergistic relationship between certain of the vegetable sterols and the polyunsaturated fatty acids.

Other investigators suggest the possibility that unknown materials present in trace amount in natural fats may be responsible for lowering the plasma-cholesterol level. Such a hypothesis seems unnecessary in view of the evidence presented here.

Keys et al. (1957), on the basis of somewhat unconvincing data, and Ahrens et al. (1957), from observations with natural fats containing considerable quantities of oleic acid, have advanced the hypothesis that double bonds furnished by fatty acids are responsible for the effects observed—i.e., sufficient oleate would be quite as effective as linoleate or arachidonate. Our studies do not support such a hypothesis.

In view of the ease with which oleate can be formed from carbohydrate and other entities, such a hypothesis would not seem tenable in any event. Mead's (1957) studies indicate that oleic acid is metabolised quite differently from linoleic acid. One may anticipate that this picture will come into much sharper focus within the next year. It is our impression, however, that the amount of linoleic acid required to "balance" a given amount of oleic acid may be less than that required for an identical amount of stearic or of palmitic acid. Work designed to assess this statement further is in progress.

Earlier in this paper the question was raised: "Is information available about the mechanism of depression of the plasma-cholesterol level by essential fatty acids?" Increased excretion of cholesterol might conceivably be an explanation. This seems unlikely to us (at least as an explanation of the major portion of the effect) for the following reasons:

(1) It subscribes to the long-standing, perhaps naïve, philosophy that cholesterol is "bad" and must be exorcised.

(2) The excretion pattern observed in different people is unpredictable and bears no necessary relationship to the changes in blood levels.

More probably, the effect of essential fatty acids is by regulating the production of cholesterol. A final explanation has not yet been found, but the following is a working hypothesis which has been changed but little since 1955.

Since the reports of Stetten and Boxer (1944) and Stetten and Klein (1945) many other reports have been published supporting the concept that fat is the "prime fuel" of the body. This is probably so, regardless of the dietary intake. A low-fat diet inevitably is a high-carbohydrate diet. Under most conditions the greater portion of ingested carbohydrate is probably transformed to fatty acids in the fat depots and eventually mobilised and metabolised through fatty-acid pathways. Conse-

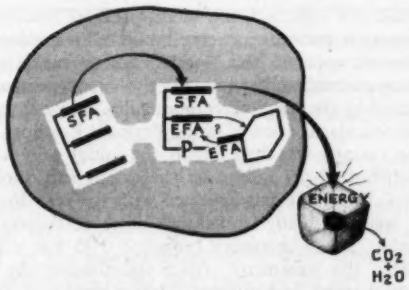

Fig. 4—Transport of fatty acids: glycerids carry bulk of fuel fatty acids; lecithin is the most metabolically active transporter of fuel fatty acids; turnover of saturated fatty acids (S.F.A.) is much more rapid than the turnover of remainder of lecithin molecule.

quently two major problems exist—how fatty acids are transported and how they are rendered soluble.

In round figures, a 6-ft. man indulging in normal activity transports and utilises about 1 mol of fatty acid, nearly 300 g. (computed as C_{18} acid) in twenty-four hours. After a meal the plasma-lipid level in healthy people is higher than 700 mg. per 100 ml. Of this total lipid about 60% is fatty acid (glyceride, phospholipid, &c.). Because of the very limited aqueous solubility of most of these lipids and the toxicity of those compounds which are somewhat soluble (e.g., sodium oleate and certain mono- and di-glycerides) protein adsorption of lipids becomes an overwhelming necessity. A series of "lipoproteins" exists, ranging from the high-density small-molecule albumen-fatty-acid complex (almost entirely protein) through the α and β lipoproteins to the low-density large-molecule chylomicrons (almost entirely fat, just enough protein to prevent coalescence of fat-droplets and consequent embolism). None of the foregoing sheds any light on the need for essential fatty acids.

In healthy people the fatty acids which make up the plasma neutral fats are predominantly saturated and mono-unsaturated. The most abundant plasma-phospholipid lecithin contains one non-essential and one essential fatty acids (Deuel 1951). The fatty acids esterified with cholesterol are predominantly unsaturated under normal conditions (Kelsey and Longenecker 1941). As shown in fig. 4, we conceive of triglyceride as the donator of "fuel" fatty acid, phospholipid as the most metabolically active transporter of fuel fatty acid, "cholesterol ester" as a donator of essential fatty acid for new phospholipid synthesis, and essential fatty acid as a most important part of the phospholipid molecule, perhaps in terms of "key-in-lock" enzymatic specificity. Under usual conditions the turnover of the non-essential fatty-acid portion of the phospholipid is extremely rapid; the turnover of the remainder of the lecithin molecule is quite slow. Normally, therefore, the same molecule of essential fatty acid is conserved and re-utilised many times.

If this theory is correct, the mechanism of lowering of the plasma-cholesterol level by essential fatty acid may be by way of decreased synthesis of cholesterol as the result of increased efficiency of the systems involved. The results of some experiments on animals are in accord with this interpretation (Wood and Migicovsky 1956). Conversely, in the presence of a deficiency of essential fatty acid there may be increased production of cholesterol and phospholipic, raised levels thereof in the plasma, and increased tendency to their abnormal deposition. We again emphasise that this is an oversimplified working hypothesis which undoubtedly will undergo modification as further knowledge accumulates. The fact that, for the present, it neglects the role of essential fatty acids in cellular structure in no way implies that this aspect of the biochemistry of essential fatty acids is not of tremendous importance.

There is no possible substitute for long-term clinical and chemical observation to determine whether diets relatively or absolutely rich in essential fatty acids have major value in the prevention or the treatment of atherosclerosis. We have noted the available evidence which indicates that such diets are not harmful and may, in some people, produce desirable effects. If further observations are in agreement, the concepts advanced by Sinclair (1956) regarding the pathogenesis of atherosclerosis will deserve most serious consideration, with particular reference to the role of food processing. If it is possible to improve existing vascular disease by diet, much lesser dietary modification should have significant prophylactic value. In support of this concept one notes the smaller proportion of dietary linoleic acid to saturated fat and saturated fat precursors required to lower the plasma-cholesterol level in healthy young people.

Summary

The addition of purified ethyl and glycerol esters of linoleic acid to the diet lowers the plasma-lipid levels in healthy and in unhealthy people. The addition of oleic-acid preparations does not do this.

On the basis of these and earlier observations it can be concluded that the major active ingredient in various vegetable fats responsible for lowering the plasma cholesterol is linoleic acid.

Results obtained with a phosphatide mixture containing arachidonic acid suggest that this acid may be much more potent, gramme for gramme, in lowering the plasma-cholesterol level than is linoleic acid, at least under the conditions noted.

There is some evidence that palatable mixed diets rich in essential fatty acids, in addition to lowering the plasma-cholesterol level, are also associated with clinical improvement in patients with arterial degenerative disease.

Evidence is presented that the prescription of a low-fat diet is biologically unsound.

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PENTACYNIUM BIS-METHYLSULPHATE (PRESIDAL) IN THE MANAGEMENT OF HYPERTENSION

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Locket (1956) reported preliminary results obtained with two members of a group of ganglion-blocking agents in which there was an apparent dissociation between hypotensive activity and the ability to produce ocular changes and gastrointestinal disturbances. The most active member was 139.C.55, pentacynium or ' Presidal ', and this paper describes a clinical study of this compound given by injection and orally to a series of 30 severely hypertensive patients for periods of from three to eighteen months.

Presidal is N¹-(5-cyano-5-5-diphenylpentyl)-N¹: N¹: N² trimethylethylene - 1 - ammonium - 2 - morpholiniumbis-methylsulphate, a member of a series of unsymmetrical bisonium salts first described by Adamson et al. (1956);

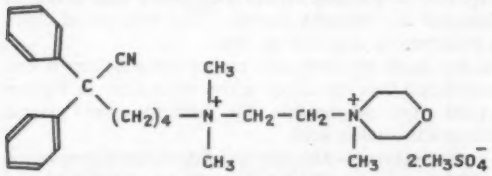

Fig. 1—Structural formula of pentacynium bis-methylsulphate.

its structural formula is shown in fig. 1. The chemistry of this compound and its close analogues has been described by Billinghurst (1956), and its pharmacology has been reported by Green (1956).

Material and Method

Selection of Cases

The group of patients studied comprised 30 consecutive admissions for severe hypertension to the wards of the Liverpool Regional Cardiac Centre. The criteria for selection were: (1) malignant hypertension with papill-œdema, and (2) essential hypertension severe enough to produce incapacitating symptoms or serious cardiac or cerebral complications.

17 of the patients were men and 13 women. Their ages ranged from 41 to 68 with a mean of 55. The length of history of hypertensive symptoms varied from two weeks to ten years. On the Keith et al. (1939) classification of the severity of hypertensive disease based on fundal changes, 6 fell into group IV, 8 into group III, and the remainder into group II. Gross dyspnœa was present in 19; and 28 of the 30 patients had electrocardiographic evidence of myocardial disease or severe left-ventricular strain. 5 had already had an attack of myocardial infarction, and 8 had had a cerebral thrombosis or subarachnoid hæmorrhage.

Method

On admission the hypertension was fully investigated and the patient's cardiac, renal, and cerebral condition assessed. A test dose of pentacynium was then given by subcutaneous injection, and blood-pressure readings were taken over a period of twelve hours. To maintain uniformity throughout this series and to make possible comparison with other series, the blood-pressure was measured by the method recommended by the Committee for the Standardisation of Blood Pressure Readings (1939).

Oral therapy was then begun, the initial daily dose and its distribution depending on the extent and duration of the blood-pressure fall obtained with the test dose. The dose was gradually increased until stabilisation was obtained. In 13 instances reserpine 0·25 mg. t.d.s. was added to the treatment. After stabilisation the patient was discharged and followed up monthly in the out-patient clinic.

Results

Blood-pressure Response to a Single Dose

All patients except 1 showed a significant fall in the supine systolic and diastolic blood-pressures when given a subcutaneous test-dose of pentacynium, which ranged from 3 to 10 mg. The degree of blood-pressure fall varied with the dose given. 10 mg. produced a mean systolic fall of 90 mm. Hg and a diastolic fall of 40 mm. in the supine position; 3 mg. produced a mean systolic fall of 70 mm. and a mean diastolic fall of 30 mm. The blood-pressure started to fall on an average ten minutes after injection and reached its lowest level after one to one and a half hours. It remained at this level for several hours and then rose slowly to its initial height in six to twenty-four hours, with a mean of twelve hours. In the standing position there was greater hypotension, and in the trough of the blood-pressure fall hypotensive symptoms were often present. A typical blood-pressure response after a test dose of pentacynium is shown in fig. 2.

Intravenous administration produced a greater and more rapid fall of blood-pressure than did subcutaneous or intramuscular injection. The action began within five minutes, and the trough of the blood-pressure fall was reached in fifteen to twenty minutes. After oral administration, the blood-pressure began to fall after twenty to thirty minutes and the effect was greatest about an hour later. After both oral and parenteral administration, the greater the blood-pressure fall the longer was its duration. Postural hypotension sometimes persisted for some hours after the pressures in the supine position had returned to control levels.

In most cases there was moderate slowing of the heart-rate. The reduction was generally about ten to fifteen beats a minute, and this effect coincided closely with the hypotensive effect of the drug (fig. 3). Pentacynium also

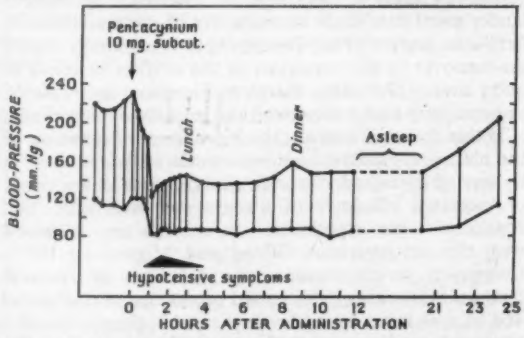

Fig. 2—Blood-pressure response after test dose of pentacynium (patient supine).

inhibited the homœostatic vasoconstrictor impulses and abolished or greatly reduced the blood-pressure overshoot which normally follows the Valsalva manœuvre.

Relative Potency of Parenteral and Oral Pentacynium and Other Ganglion-blocking Agents

The potency of the parenteral and oral forms was compared in 28 patients. The effective oral dose was from ten to twenty times the effective subcutaneous dose; and this ratio varied from patient to patient, depending mainly on the time-relationship between administration of the oral dose and the main meals of the day.

Parenterally, pentacynium was found to be about equipotent with chlorisondamine and mecamylamine, and two to three times as potent as pentolinium. Orally, it was as potent as chlorisondamine, twice as potent as pentolinium and about a tenth as potent as mecamylamine.

Factors Influencing Hypotensive Action

The fall in blood-pressure after pentacynium, like that after other ganglion-blocking agents, was greatest when standing, least when lying, and intermediate when sitting. In 5 of the 30 patients there was an excessive postural fall, particularly during the period of stabilisation. The effect of posture on the blood-pressure levels is shown in fig. 3. As with hexamethonium (Smirk and Alstad 1951), pentolinium (Smirk 1953), chlorisondamine (Smirk and Hamilton 1956), and mecamylamine (Smirk and McQueen 1957), a meal taken during the course of action of pentacynium produced an additional fall in blood-pressure. This postprandial fall was generally 20–40 mm. Hg systolic; it began within an hour of the meal and lasted up to two hours. This effect is shown in figs. 2 and 3. However, in no instance was the postprandial fall greater than the post-injection fall of blood-pressure. Vasodilatation due to alcohol or an increase in room-temperature also increased the hypotensive effect, as with other ganglion-blocking agents.

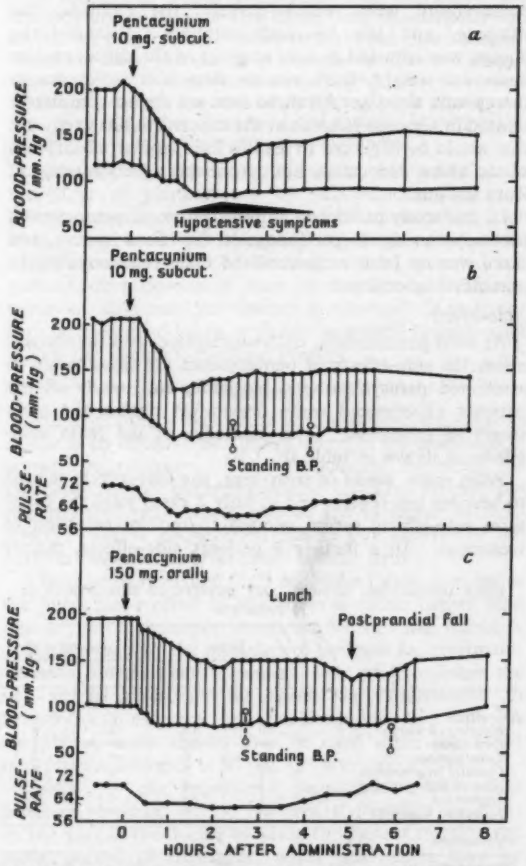

Fig. 3—Blood-pressure response to pentacynium: (a) test dose of 10 mg.; (b) test dose of 10 mg. after 9 months' treatment; (c) oral dose of 150 mg. on empty stomach.

TABLE I—MEAN AND RANGE OF BLOOD-PRESSURE FALL WITH A DOSE OF PENTACYNIUM IN PATIENTS WHO HAD PREVIOUSLY RECEIVED PENTOLINIUM, MECAMYLAMINE, OR NO TREATMENT

Previous treatment	Dose of pentacynium (mg.)	No. of cases	B.P. fall (mm. Hg)	
			Mean	Range
None	10	11	85/35	35/20–150/70
Pentolinium ..	10	5	100/45	85/35–120/60
Mecamylamine ..	10	4	85/35	60/10–100/50

Tolerance and Cross-tolerance

In the first few days of treatment tolerance developed in 13 of the 30 patients. To produce a similar fall of blood-pressure on consecutive days, the dose had to be increased by 10–20%. In the remainder there was little evidence of tolerance, and the fall in blood-pressure obtained by repeating the test dose after many months was similar in extent and duration to that produced by the initial test dose (see fig. 3).

After stabilisation it was rarely necessary to increase or decrease the total daily dose; but change in the patient's occupation or daily routine, or in the weather, sometimes necessitated alterations in the distribution of the daily dose.

Cross-tolerance between pentacynium and other ganglion-blocking agents was not evident in this study. No significant difference was found in the mean fall in blood-pressure after a constant dose of pentacynium between the previously untreated group and those who had been treated with pentolinium or mecamylamine (table I). A minor degree of cross-tolerance could not be excluded, however, for there was in most cases an interval of a week or more between the cessation of therapy and the administration of a test dose of pentacynium.

Results of Long-term Oral Therapy

30 patients were treated by mouth for periods of from three to eighteen months. The initial oral dose given was generally 50 mg. three times daily, and this was increased by 25 mg. every two days until an adequate response was obtained or until side-effects—generally blurred vision or postural hypotension—prevented further increase. Response to treatment was classified according to the average supine diastolic pressure. If this was maintained at less than 110 mm. Hg, the patient was regarded as a responder, and, if not, a non-responder. On this basis 24 were classified as responders at the time of assessment, and 6 as non-responders (table II). A typical response to long-term therapy is shown in fig. 4.

TABLE II—MEAN BLOOD-PRESSURES BEFORE AND DURING TREATMENT WITH PENTACYNIUM IN RESPONDERS AND NON-RESPONDERS

Group	No. of cases	Pretreatment B.P. (supine)	B.P. levels during treatment	
			Supine	Standing
Responders ..	24	235/135	165/95	140/90
Non-responders ..	6	255/140	230/130	225/135

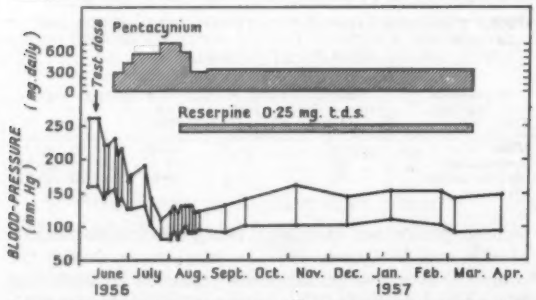

Fig. 4—Blood-pressure response to long-term oral pentacynium and reserpine (0.25 mg. t.d.s.) therapy.

In the group of responders the total daily oral requirement of pentacynium varied from 300 to 700 mg. (mean 375 mg.). This was generally given as three doses, before breakfast (7 A.M.), before tea (3 P.M.), and before retiring (9 P.M.). In some cases twice-daily administration was found to be sufficient, and in 1 case four doses daily were necessary. Absorption was best on an empty stomach, and for this reason the before-breakfast requirement was often smaller than the afternoon and evening doses.

After discharge most patients were encouraged to return to work as soon as possible and were instructed to keep rigidly to their scheme of treatment. After a few weeks some patients knew without recourse to blood-pressure readings whether their hypertension was still under control, and some were able to suggest useful improvements to their daily regimen of treatment.

Relief of Symptoms and Regression of Signs

Such symptoms as breathlessness on exertion, headaches, nausea and vomiting, and angina were rapidly relieved as the blood-pressure was lowered, and in most cases there was obvious regression of the signs of hypertensive disease.

Where congestive heart-failure was present before treatment, this improved. The heart size was often reduced and the clinical and electrocardiographic evidence of left ventricular strain became less.

Retinal hæmorrhage and exudate disappeared and papilloedema slowly regressed, though in only 1 case out of 6 did it entirely disappear.

Exercise Tolerance during Treatment

When exercise tolerance had been seriously reduced by hypertensive disease, it improved greatly when the blood-pressure was lowered. A patient who, when first seen, could walk only a few yards without gross dyspnœa was able, after seven months' treatment with pentacynium alone, to walk 500 yards without undue effort. In hypertensive patients the blood-pressure often rises sharply during exercise; pentacynium prevented this. In several patients under treatment the diastolic pressure fell during exercise, particularly when this involved mainly the leg muscles.

Value of the Test Dose

A patient who had a good response to a parenteral test dose did not always do well on long-term oral treatment, but a patient who responded poorly to an adequate test dose invariably did badly.

Combination with Reserpine and other Drugs

As with hexamethonium, pentolinium, chlorisondamine, and mecamylamine, introduction of the alkaloids of rauwolfia into the treatment produced an additional fall in blood-pressure. On average (13 patients), reserpine 0·25 mg. t.d.s. further lowered the systolic and diastolic blood-pressure, both in the supine and standing positions, by approximately 10–20 mm. Hg. Unlike that caused by the ganglion-blocking agents, this additional fall did not depend mainly on posture, and affected the systolic and diastolic pressures to a similar extent. In this respect our findings agree with those of Cooper and Cranston (1957). The close agreement between the degree of lowering of blood-pressure by reserpine alone obtained by these workers and the additional lowering in blood-pressure obtained in our series by adding reserpine to ganglion-blocking therapy strongly suggests that the effects of these drugs are additive and not synergistic.

Cessation of pentacynium therapy while reserpine was continued caused the systolic and diastolic pressures to revert to within 20 mm. Hg of their control levels.

The introduction of reserpine into therapy enabled the dose of pentacynium to be reduced in some cases. The incidence of side-effects was thereby lowered and more effective control of the blood-pressure achieved. Reserpine caused no depression.

Effect of Anion on Activity

Harington and Rosenheim (1954) reported that the oral absorption of hexamethonium depended to some extent on the anion. In this investigation three salts of pentacynium were tested—namely, the chloride, the sulphate, and the bis-methylsulphate. Provided the dosage was adjusted to take account of the differences in molecular weight, there was no detectable difference in therapeutic activity. All three salts are almost completely ionised in aqueous solution at the concentrations used, and this would be expected to lead to independent absorption of the anion and cation both from the injection-site and from the gut.

In this study prolonged administration of pentacynium produced no significant change in the blood picture, and there was no local or generalised toxic reaction after its parenteral or oral use.

Side-effects

As with pentolinium, chlorisondamine, and mecamylamine, the side-effects of pentacynium are due mainly to associated parasympathetic blockade, and nearly all the patients experienced some discomfort during the early stages of treatment. The incidence of the main side-effects is shown in table III.

After some weeks of treatment, the side-effects tended to become less severe, and in only 3 cases were the long-term side-effects severe enough to require cessation of treatment. In a further 9 patients side-effects, mainly

TABLE III—NATURE, NUMBER, AND SEVERITY OF SIDE-EFFECTS IN 30 PATIENTS

—	Early		Late	
	Severe	Mild	Severe	Mild
Side-effects:				
Blurring of vision	10	13	1	6
Dry mouth	—	11	—	1
Constipation	—	5	—	2
Postural hypotension	2	5	—	2
Nausea and vomiting	1	4	—	2
Impotence	1	—	1	—
Muscular weakness	—	2	—	—
No symptoms	3		18	
Inconvenience	24		9	
Disabling symptoms	3		3	

blurring of vision and postural faintness, persisted and gave rise to some discomfort, though they were not severe enough for the patient to demand the stopping of treatment.

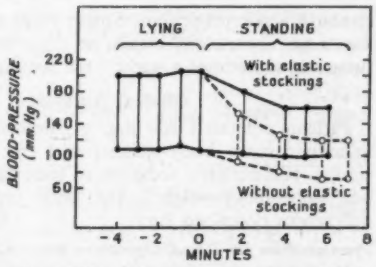

Fig. 5—Effect of elastic stockings on blood-pressure fall in standing position.

Control of side-effects.—Blurring of vision was controlled by one drop of 0·1% pilocarpine instilled into the conjunctival sac once or twice daily. Constipation, when it occurred, was treated with laxatives. 1 patient, who occasionally had severe symptoms of postural hypotension but whose dose it was considered unwise to reduce, was greatly helped by wearing elastic stockings, which reduced the postural fall in blood-pressure (fig. 5).

Comparison and Scheme of Treatment

Comparison with other ganglion-blocking substances was possible in 10 patients—with pentolinium in 5 and with mecamylamine in 5.

3 patients in whom pentolinium had previously been discontinued because of side-effects were satisfactorily controlled on pentacynium; the other 2 showed little change in control of blood-pressure or in side-effects. Of the 5 patients who also received mecamylamine, 3 were classed as non-responders to both this and pentacynium; 1 was equally well controlled with either drug; and 1 had a smaller blood-pressure fall and fewer side-effects with mecamylamine.

Although each patient in this study received an initial test dose of pentacynium by subcutaneous injection, there appears to be no reason why treatment should not start with a small oral dose of 50 mg. two or three times daily, provided the blood-pressure can be recorded frequently; this dose may then be increased by 25 mg. every two days until stabilisation is achieved. If reserpine is to be used in addition, it should be started about a week before the ganglion-blocking therapy.

Discussion

Our preliminary experience with pentacynium suggests that it is an effective and useful agent in the treatment of severe hypertension. The dissociation between the sympathetic and parasympathetic blocking actions has redistributed rather than reduced the incidence of side-effects. Severe constipation has in our experience not been as common as with other similar drugs.

The dose of reserpine (0·25 mg. t.d.s.) used to enhance the hypotensive effect in this study is rather higher than that at present generally recommended (0·1 mg. t.d.s.).

With regard to the selection of patients for treatment, we consider that in the present state of knowledge the use of ganglion-blocking agents is unjustifiable in symptomless essential hypertension, and that only in exceptional cases should they be used when the blood non-protein-nitrogen is 50 mg. or more per 100 ml.

Finally, in our experience pentacynium, like other ganglion-blocking agents, requires a considerable effort on the part of the doctor to guide the patient through the initial period of treatment, when side-effects may be troublesome. Success in the treatment of hypertension with ganglion-blocking agents depends more on the doctor's management of the patient than on the use of any individual drug.

Summary

Pentacynium bis-methylsulphate ('Presidal') was administered by injection and orally to 30 hypertensive patients for periods of up to eighteen months.

The blood-pressure was adequately controlled in 24 of these 30 cases. Reserpine 0·25 mg. t.d.s. increased the hypotensive effect by 10–20 mm. Hg.

The side-effects were similar to those of other ganglion-blocking substances, but constipation was less severe.

We thank Dr. E. Noble Chamberlain and Dr. Robert Coope for their interest, advice, and help, and the consultant physicians, registrars, house-physicians, sisters and nurses of the Sefton General Hospital, Liverpool, for their ready cooperation. The material used in this investigation was supplied by Burroughs Wellcome & Co.

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METHYLPENTYNOL CARBAMATE
PHARMACOLOGICAL AND CLINICAL INVESTIGATIONS

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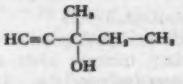
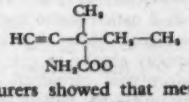
IN the search for a drug as innocuous as methylpentynol (Trotter 1953, Bourne 1954, Gusterson 1955) methylpentynol carbamate was produced.

Methylpentynol



Methylpentynol carbamate



Investigations by the manufacturers showed that methylpentynol carbamate has an oral LD_{50} in mice of 337 mg. per kg. (limits 320–348 mg.). An intravenous dose of 0·01 g. had no effect on blood-pressure or respiration in the cat or rabbit, and doses of 50 mg. per kg. had no analgesic properties in mice when tested by the hot-stage method.

No gross lesions were found at necropsy in mice which had had the drug by mouth for five months at two dose levels (170 and 85 mg. per kg. daily).

Results of metabolic experiments by us using the method of Perlman and Johnson (1952) were inconclusive; but they did indicate that methylpentynol carbamate may be rapidly metabolised by the liver, kidney, and brain tissue in vitro; and the liver and kidney seemed to be more effective than the brain.

Investigations on Volunteers

Respiratory System

6 volunteers recorded their respiratory-rates and minute-volumes by breathing into a gas-meter B.M.C. apparatus (McKerrow 1953), using a Parkinson and Cowan gas-meter calibrated in litres. Readings were obtained at four-minute intervals for twelve minutes before administering 200 mg. of methylpentynol carbamate in a single dose, and subsequently at frequent intervals for ninety minutes. 4 patients, who had received doses of 100 mg. per stone body-weight as premedication, were similarly tested. No significant alteration in respiratory-rate or minute-volume was demonstrated in any of the 10 subjects.

Cardiovascular and Hæmopoietic Systems

(*a*) 3 subjects who had doses of 100 mg. per stone body-weight as premedication had electrocardiograms recorded before taking the drug and at intervals of thirty and sixty minutes afterwards. No significant changes were seen.

(*b*) 6 healthy volunteers received 200 mg. of methylpentynol carbamate. Their blood-pressures were taken at five-minute intervals for twenty minutes before administration and every ten minutes for sixty minutes afterwards. There was no significant alteration in either the systolic or the diastolic pressure. 26 adults received 100 mg. per stone body-weight of methylpentynol carbamate before anæsthesia. Those whose blood-pressures were within the normal range showed no change. In hypertensive patients the systolic fall (20–50 mm. Hg) which usually follows premedication was observed.

(*c*) 4 healthy volunteers were given 100 mg. night and morning for ten days to see whether there was any cumulative toxic effect. Red, differential white, and platelet counts were taken the day before medication, on the fourth day, and the day after it was stopped. The counts were unchanged.

Liver Function

The same volunteers were seen before breakfast on four occasions—the day before medication, the fourth and eighth days of medication, and the day after medication was stopped. 15 ml. of blood was withdrawn at each visit by a self-retaining venous cannula, which was then sealed and left in situ. Sulphobromophthalein (5 mg. per g. body-weight) was injected into a vein in the opposite arm, and at twenty and forty minutes later, 10 ml. of blood was withdrawn through the cannula for plasma-dye estimations. 10 ml. of the original specimen was used as a control for the sulphobromophthalein test, the remainder being used for the van den Bergh and serum-alkaline-phosphatase tests. The results of these tests suggested that the liver was unaffected by the medication.

Kidney Function

Daily specimens of urine from the 4 volunteers were analysed and examined microscopically. No abnormality was found.

Electroencephalogram

Electroencephalograms were recorded in 5 volunteers before and sixty minutes after a preoperative dose of 100 mg. per stone body-weight. The readings were compared with those in 2 patients who had pentobarbitone (gr. $^1/_2$ per stone body-weight). After barbiturates there was an increase in fast activity similar to that associated with deep sleep. With methylpentynol carbamate there was little increase in fast activity unless the patient did fall asleep.

Reaction-time and Muscular Coordination

Tests were carried out, using methylpentynol carbamate, similar to those described for methylpentynol (Trotter 1954). Results were of the same order. As with methylpentynol reaction-times after methylpentynol carbamate were *decreased* (not increased as after alcohol or pentobarbitone). Muscular co-ordination tests were normal. (Apparatus used: McDougal-Schuster dotter apparatus and motorcar cockpit supplied by the Royal Society for the Prevention of Accidents.) (Moreover, the drug has been administered by us to over 10,000 ambulant patients, with no apparent impairment of reaction-time.)

These preliminary investigations disclosed no side-effects, but we ourselves took increasing doses to try to establish a safe maximum. Single doses of 1200 mg. produced no drowsiness, ataxia, or digestive upset, though there was sometimes a slight "hot feeling" in the gullet.

Clinical Studies

Patients tolerated 100 mg. of methylpentynol carbamate per stone body-weight; and this dose produced similar preoperative sedation to pentobarbitone (gr. $^1/_2$ per stone body-weight), but with certain qualitative differences described later.

Premedication for Dental Operations under Local Anæsthesia

Methylpentynol carbamate was given to over 10,000 ambulant outpatients in the following dosage :

Patients without visible sign of apprehension ..	2 × 100 mg. tablets
Mildly apprehensive patients	4 × 100 mg. tablets
Very apprehensive patients	100 mg. per stone body-weight

Children were given up to four tablets routinely, but those who were very apprehensive or uncontrollable were given higher doses, proportional to body-weight, without untoward effect.

Of the 10,000 patients thus treated, 90% showed no apprehension during operation, 7% were apprehensive, and 3% were very apprehensive. In some of the patients in the last two groups (7% and 3%) the dose was augmented to 100 mg. per stone body-weight (if a smaller dose had previously been given) immediately their apprehension was apparent after the start of the operation. After a suitable pause the operation began again, and their apprehension was then removed or much reduced. Hilarity and loquacity, occasionally noticed with methylpentynol (Trotter 1954), were negligible.

Methylpentynol carbamate took longer to act than methylpentynol, but the effect lasted longer. This is an advantage when operations are long. or when postoperative sedation is needed. The delayed onset may be a disadvantage when the drug is given to a patient at the surgery; but, if taken before the patient left home, methylpentynol carbamate could conceivably relieve the "waiting-room" apprehension and still be effective during the operation.

Premedication in Ambulant Patients before Dental Extractions under General Anæsthesia

The 373 patients in this group consisted of those who showed much apprehension on arrival; those who were accustomed to premedication; those who, after settling in the dental chair, resolutely refused the anæsthetic; and children with a history of toothache who had been so upset that intra-oral examination on admission was impossible.

31 received elixir of methylpentynol orally (250–750 mg.); 40 received methylpentynol carbamate orally (200–1000 mg.); 82 received methylpentynol carbamate orally and hyoscine (gr. $^1/_{300}$–$^1/_{150}$) sublingually; and 63 received hyoscine alone.

Further comparisons were afforded by 101 patients who received pentobarbitone orally (gr. $^1/_8$–$2^1/_2$); 13 who had pentobarbitone orally and hyoscine (gr. $^1/_{300}$–$^1/_{150}$) sublingually; 14 who had pethidine intravenously (20–34 mg.); 26 who had chloral hydrate orally (gr. 5–8); 2 who had phenobarbitone sodium orally (gr. 1); and 1 who had promethazine-8-chlorotheophyllinate ('Avomine') 50 mg. orally and hyoscine gr. $^1/_{150}$ sublingually.

Pentobarbitone (gr. $^1/_2$ per stone body-weight), used for years, has been discarded by some anæsthetists because it caused a great deal of ataxia and sleepiness during recovery. A dose of gr. $^1/_4$ per stone combined with sublingual hyoscine (gr. $^1/_{150}$–$^1/_{75}$) solved this problem, but failed to provide adequate sedation. On this dosage the average time between recovery and going home was over forty-four minutes (13 cases), whereas with methylpentynol carbamate and hyoscine this was reduced to under twenty-seven minutes (82 cases).

Methylpentynol had the disadvantage, with general anæsthesia, that it had to be taken with water (or fruit-juice) only a quarter or half an hour before induction, and occasionally there was vomiting. Methylpentynol carbamate eliminates this disadvantage, for it can be given an hour or more beforehand.

REACTION TO INTRAVENOUS INJECTION IN CHILDREN (INDUCTION OF ANÆSTHESIA)

Premedicants	No. of cases	Flinch	Withdrawal	Struggle	Gas given before intravenous injection
Pentobarbitone and atropine	89	33 (37%)	29 (33%)	27 (30%)	33 (37%)
Pentobarbitone and hyoscine	26	10 (38%)	8 (31%)	8 (31%)	10 (38%)
Methylpentynol carbamate and atropine	21	8 (38%)	1 (5%)	0	2 (10%)
Methylpentynol carbamate and hyoscine	36	12 (33%)	0	0	3 (8%)
Papaveretum and hyoscine	28	4 (14%)	0	0	1 (4%)

As hyoscine reinforces the action of pentobarbitone, it was used with methylpentynol carbamate. It was given sublingually in tablet form in doses of gr. $^1/_{150}$ to children up to the age of 12 years and gr. $^1/_{75}$ to those above this age. With this regimen, sedation was seen at its best. Patients who had been agitated, apprehensive, or completely unmanageable sat down quietly and, for the most part, accepted induction with complete equanimity. Nearly 80% of these had refused to have gas only sixty to ninety minutes previously.

Only 5 patients who had methylpentynol carbamate were sleepy on recovering from the anæsthetic.

Premedication before General Surgical Operations under General Anæsthesia

Methylpentynol carbamate, with either hyoscine or atropine, was given to 96 children (age 2 to 14 years) for tonsillectomy and adenoidectomy or both, and the results were compared with those after pentobarbitone premedication, which has been given previously for these operations. In addition, 26 adults were premedicated with methylpentynol carbamate and hyoscine before various operations. In all these cases the methylpentynol carbamate was given by mouth and the hyoscine by subcutaneous injection.

In 42 tonsillectomies, methylpentynol carbamate was given at varying times before operation; the effect was greatest between one and two hours after administration. Preoperative cooperation was good in 33, poor in 8, and bad in 1. 9 arrived at the anæsthetic room asleep. Of the 8 in whom cooperation was poor, 5 had received their methylpentynol carbamate four hours previously, 2 three hours previously, and 1 two hours previously. Subcutaneous atropine (gr. $^1/_{100}$) was administered three-quarters of an hour before operation.

In 54 tonsillectomies, atropine was replaced by hyoscine (gr. $^1/_{300}$) subcutaneously. Cooperation was good in 49, poor in 4, and bad in 1. Of the 4 with a "poor" response, 3 had received methylpentynol carbamate four hours previously, and 1 one hour previously.

In these two series only 28% of the children and 15% of the adults were restless during recovery from anæsthesia. In a control series, using pentobarbitone premedication, 93% of 148 patients were restless.

When methylpentynol carbamate is used, the recovery is hastened compared with that from pentobarbitone, and the protective throat-reflexes are soon in operation. The likelihood of blood being inhaled after tonsillectomy or other operations within the mouth is minimised, and less nursing-time is taken up in looking after semiconscious children.

Papaveretum and hyoscine gave the best results, and most adverse reactions were seen when pentobarbitone was used, though hyoscine, when added, gave slightly better results than atropine. Pentobarbitone cannot be relied on to make children accept intravenous anæsthesia, and for those who are still averse to giving papaveretum to children methylpentynol carbamate offers an attractive alternative. At the preoperative follow-up injection of atropine or hyoscine after methylpentynol carbamate, slight flinching was the rule, there was no withdrawal or struggling. This lack of response to needle-prick has an added advantage in that only one nurse is needed to give the preoperative follow-up injection of atropine or hyoscine, which is not true of barbiturate premedication.

Discussion

As a general rule the barbiturates seem to act in two ways: they depress certain inhibitory mechanisms, so increasing the reflex irritability of the greater part of the central nervous system, and they depress the reticulo-activating centre, so causing loss of consciousness. With barbiturates, an increased nervous irritability is shown by an exaggerated response to painful stimuli, a tendency to laryngospasm, and restlessness during recovery. Some barbiturates are central convulsants, with no hypnotic properties whatever (Cope and Hancock 1939, Knoefel 1945).

After barbiturates, withdrawal or struggling is the usual reaction to an intravenous needle, but after papaveretum or methylpentynol carbamate the patient rarely reacted adversely (see table). Either methylpentynol carbamate is to some extent analgesic, or it provides a central nervous sedation in contrast to the increased nervous excitability produced by the barbiturates. The fact that hypnosis is rare with methylpentynol carbamate deceives those accustomed to using barbiturates into assuming that the sedative powers of methylpentynol are less than they really are; but the use of methylpentynol carbamate 800 mg. three-hourly in childbirth has led to the suggestion that in high dosage it may be analgesic (Barnett, personal communication).

We have not seen laryngeal spasm after giving methylpentynol carbamate, except in the pilot investigation when some patients were given the drug as long as two and a half to four hours before anæsthesia. This is in sharp contrast to those given barbiturates. Methylpentynol carbamate, therefore, provides a much easier changeover to ether after induction with nitrous oxide and oxygen, and laryngospasm is rare during those throat operations when light anæsthesia is maintained and an endotracheal tube is not used. The drug does not cause respiratory depression, so it is safer to use intravenous anæsthesia after methylpentynol carbamate than after barbiturates.

Conclusions

Results of tests with methylpentynol carbamate, and observation of over 10,000 patients to whom the drug was given, suggest that it has low toxicity and no undesirable side-effects.

The delayed onset and longer action of methylpentynol carbamate have many advantages, but they become disadvantageous when a rapidly acting short-duration drug is needed. Methylpentynol itself is then the drug of choice.

We should like to thank Prof. C. H. Gray, Dr. E. D. Lawrence, Dr. W. M. Davidson, and Dr. S. Nevin for their help. Our thanks are also due to Miss M. Hall, Dr. Margaret Rooms, Dr. William T. Henry, Dr. N. Tate, Miss O. Jenkins, Mr. G. H. Wilkinson, the students of King's College Hospital who took part in the tests, and the sisters and nurses at various hospitals for their cooperation. British Schering, Ltd., supplied the methylpentynol carbamate ('Oblivon-C').

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METHYLPENTYNOL CARBAMATE AND LIVER FUNCTION

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METHYLPENTYNOL carbamate (methyl 1-3-pentyne-1-ol-3 carbamate) is a recently introduced derivative of methylpentynol ('Oblivon'), its pharmacology having been studied by Halpern (1956) and Halpern and Lehmann (1956) and a clinical appraisal coming from Kourilsky and Kourilsky (1957).

Schaffarzick and Brown (1952) had produced evidence that methylpentynol was potentially hepatotoxic, but Kennedy and Trounce (1955) averred that it had no untoward effect on liver function. Nevertheless, since the carbamate is stated to be three or four times as potent as the parent substance, we considered it worth while to exclude any possibility of an adverse action on the liver.

Methods

12 patients (7 male and 5 female), aged 28–49, weighing 33·6–88·2 kg., and having various diseases, were therapeutically prescribed methylpentynol carbamate 1–3 g. daily for two to seven weeks, no other drugs being concurrently administered. Patients likely to be exceptionally susceptible to drugs—e.g., those with anæmia, and those with either a history or evidence of hepatic and renal damage—were excluded.

All the patients were seen daily throughout the investigation. A battery of liver-function tests relating to excretory function and to protein metabolism were applied initially during a seven-day control period when the patient was receiving inert tablets, and thereafter weekly while methylpentynol carbamate was being prescribed, a further series of control values being obtained two weeks after the end of therapy.

The methods and values for the liver-function and other tests were as follows: bile pigments, Fouchet's test; bile salts, Hay's test; urinary urobilin, Schlesinger's fluorescence method, and urinary urobilinogen, Ehrlich's aldehyde test on an early morning specimen of urine, the results for both being graded from 0 to 4+ with a 1+ or greater regarded as abnormal; serum-bilirubin, serum treated with diazo solution followed by alcohol and saturated ammonium sulphate, a normal value being less than 1 mg. per 100 ml.; alkaline phosphatase, method of King and Armstrong, with a normal range of 3–13 units; total plasma-proteins, normal range 5·8–8·6 g. per 100 ml.; serum-albumin, 3·4–6·7 g. per 100 ml.; serum-globulin, 1·2–2·9 g. per 100 ml., preliminary separation being achieved with 26% sodium sulphate and estimation by the micro Kjeldahl method (Harrison 1949); thymol turbidity, method of Maclagan (1944), the normal range being 0–4 units, the grading of 0–4+ of Maizels (1946) also being adopted, with ± representing fine granularity without precipitation, usually over the range of 4–8 units; thymol flocculation, method of Neefe (1946), the result being graded only as negative or positive; zinc-sulphate reaction (normal, 2–8 units) by the turbidimetric technique of Kunkel (1947); cephalin-cholesterol test, with flocculation graded from 0–4+ and read at twenty-four and forty-eight hours, readings of 2+ or greater being deemed abnormal; prothrombin time (Quick's test) with thromboplastin supplied by DIFCO and done concurrently on the patient and a control; erythrocyte-sedimentation rate (E.S.R.) (Westergren), the values adopted being those suggested by Westergren (1957) of an upper limit of normality of 5 mm. at one hour for males and 12 mm. at one hour for females.

The remaining investigations such as the blood film, white-cell count and differential, hæmoglobin, and routine testing are too familiar to require amplification.

Results

No abnormalities were discovered in the tests for bile salts or pigments, urinary urobilin, serum-bilirubin, alkaline phosphatase, total plasma-proteins, serum-albumin and serum-globulin, zinc-sulphate or cephalin-cholesterol reactions, prothrombin-time, hæmoglobin values, blood film, and white-cell count and differential.

The positive abnormalities found were as follows:

Tests of Excretory Function

Urobilinogen (grading 1+) was detected in the urine of cases 8 and 11 during the final two and three weeks of the drug regime, reverting to normality two weeks after withdrawal of the carbamate. At no time was either patient pyrexial.

Tests of Protein Metabolism

A *thymol-turbidity* reading of 5 units (control value 3 units) with a ± grading was noted in cases 8 and 9 during the last week of treatment with methylpentynol carbamate. The *thymol-flocculation test* also became positive in case 12 during the final week of treatment with methylpentynol carbamate.

Other Tests

A presumed significant increase of the E.S.R. in the absence of either intercurrent illness or pyrexia was noted for 2 males: in case 9 the reading increased from a control value of 5 mm. at one hour to 15 mm. and 17 mm. at one hour during the last two weeks of treatment with methylpentynol carbamate; in case 12 the E.S.R. rose from the control value of 4 mm. at one hour to 14, 12, and 17 mm. at one hour in the last three weeks of treatment with methylpentynol carbamate.

Urine: a substance reducing Benedict's solution (blue to orange) was noted in the urine of case 12 during the last three weeks of treatment with methylpentynol carbamate.

Other Drug Effects

An unexpected high incidence of toxic effects referable to the central nervous system was also evident, the time sequence of which, together with the scheme of dosage for the drug, is depicted in fig. 1. These complications occurred in 11 cases but only when the dose of methylpentynol carbamate exceeded 1 g. by mouth daily. The individual signs and symptoms are displayed in fig. 2.

The mildest toxic phenomena amounted to behavioural changes—e.g., drowsiness, slight disturbance of mood—and

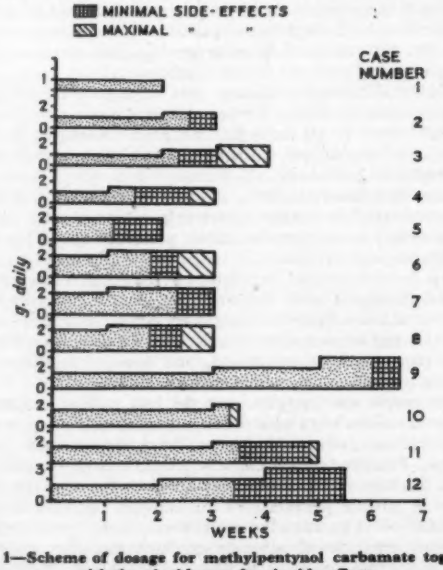

Fig. 1—Scheme of dosage for methylpentynol carbamate together with time incidence of toxic side-effects.

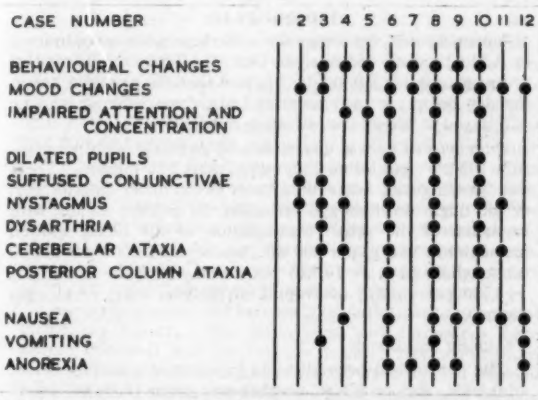

Fig. 2—Individual incidence of abnormal symptoms and signs with methylpentynol carbamate.

physical signs, including suffusion of the conjunctivæ, with nystagmoid jerks of the eyes on conjugate lateral gaze. These minimal abnormalities presented without further development and without meriting withdrawal of methylpentynol carbamate in 5 patients (cases 2, 5, 7, 9, and 12), and being the precursor to a much more dramatic picture in 5 others (cases 3, 4, 6, 8, and 11). These last-named patients displayed intense affective disturbance (symptomatic depression and irritability) combined with signs such as pupillary reflex anomalies, sustained nystagmus on conjugate lateral deviation of the eyes, diplopia, ptosis, loss of tone in the lower facial musculature, dysarthria, and tremor of the outstretched tongue. Cerebellar and posterior-column deficits and ataxy were noted in the limbs.

When it was found that these maximal toxic reactions did not abate if methylpentynol carbamate was still administered (cases 3, 4, 6, and 8), the appearance thereafter of such features was the signal for instant withdrawal of methylpentynol carbamate. It can therefore probably be inferred that, at the higher dosage levels, methylpentynol carbamate accumulates in the body.

Severe anorexia and nausea developed during treatment with methylpentynol carbamate in 7 patients (cases 4, 6, and 8–12), and even vomiting unrelated to food and presumably ascribable to methylpentynol in cases 3, 6, 8, and 12.

Full recovery invariably ensued within five days of the withdrawal of methylpentynol carbamate.

Discussion

The mild disturbance found in tests for hepatic excretory and metabolic function seems to indicate that methylpentynol carbamate can exert a toxic action on the liver. No more precise statement is feasible, because the methylpentynol was not prescribed for longer than seven weeks, and because of the extremely high dosage administered. Any indictment is therefore slender; in fact none of the test abnormalities appeared unless the patient was receiving at least 2 g. of methylpentynol carbamate daily. It therefore seems fair to remark that, if the dosage of methylpentynol carbamate does not exceed 1 g. daily, the liver-function tests are not likely to be found abnormal.

Other untoward effects of methylpentynol in large dosage were reflected in the alterations of the mental state, particularly deviations of mood, and in physical signs indicating involvement of central nervous system function, especially the cranial nerves and the cerebellar and posterior-column connections to the limbs. Similar phenomena have been observed in methylpentynol intoxications (Marley and Chambers 1956) and after ethanol (Howells 1952, 1956). No clinical side-effects have been noted with either single oral doses of 0·1–1·0 g. of methylpentynol carbamate (A. H. Galley, personal communication) or after 0·8 g. three-hourly during labour (V. H. Barnett, personal communication).

The reducing substance found in the urine of 1 patient towards the end of methylpentynol therapy was presumably a conjugate of methylpentynol with glycuronic acid, because Perlman et al. (1953) demonstrated that a breakdown product of methylpentynol was excreted in the urine as a glycuronate.

Summary

Methylpentynol carbamate was administered to 12 patients in dosages of 1–3 g. by mouth daily for from two to seven weeks.

Mild disturbances of hepatic excretory function (urinary urobilinogen) and protein metabolism (thymol turbidity and flocculation) were observed. Increase in the E.S.R. was also noted, and a reducing substance was found in the urine. There was no alteration in the blood picture.

Side-effects attributable to methylpentynol included anorexia, nausea and vomiting, alterations in the mental state, and the appearance of such signs as nystagmus, pupillary anomalies, ptosis, loss of tone of the lower facial musculature, dysarthria, and cerebellar and posterior-column ataxia.

None of these abnormalities seem likely to develop on a daily oral dose of 1·0 g. or less of methylpentynol carbamate.

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ACUTE STREPTOCOCCAL MYOSITIS

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SPONTANEOUS acute streptococcal myositis, which is occasionally found in the tropics (Manson-Bahr 1954), has seldom been reported in England, so four fatal cases seen in the postmortem room of Addenbrooke's Hospital in 1951–56 may be of interest.

Case-reports

FIRST CASE

A farmer's wife, aged 33, returned from a holiday in Scotland on Oct. 8, 1951, with a cold which caused her to lose her voice for a day or two; within a week, however, her cold had gone, and on Oct. 15 she seemed quite well. Next morning (Oct. 16) she ached all over and felt cold and shivery; after lunch she vomited twice and began to complain of pain in the left leg.

This pain increased in severity and by the evening the limb was swollen.

Next day (Oct. 17) the pain was rather less severe, but she still felt unwell, and in the afternoon she was visited by her doctor, who found that her temperature was 103°F. Arrangements were made for her to be admitted to hospital next day, but in the evening her relations noticed that she was becoming difficult to talk to and did not seem to know what was going on. The doctor was called again and sent her to Addenbrooke's Hospital as an emergency. She was admitted at 12.30 A.M. on Oct. 18 restless, dyspnœic, cold, and sweating, with radial pulses barely perceptible and very rapid (rate about 140 a minute), blood-pressure 70/40 mm. Hg, and temperature 102·6°F. Her left thigh was œdematous and hot, the skin over it being cyanotic, with a patchy lividity. Her urine contained albumin and acetone. She was given penicillin and aureomycin intravenously, but within half an hour of admission she was unconscious and apparently moribund, and at 1.55 A.M. she died.

Previous History

Since the age of 17 she had had occasional " running sores ", rather like small boils, which came out occasionally on all parts of her body. For these she received a course of penicillin injections three years before her final illness. After this she had only a few of these sores, and none recently. For about ten years she had also at times had painful lumps which appeared near joints, especially on her hands and feet, and lasted a day or two. She also had " a form of rheumatism ", with some stiffness of the limbs and joints.

Necropsy Findings

Acute suppurative streptococcal myositis of the left quadriceps femoris muscle, which was pale and abnormally soft, with the individual fasciculi of muscle-fibres separated by thin greenish-yellow pus. The purulent infiltration extended up to the groin and down to the knee. Moderate œdema but no purulent infiltration of the left leg below the knee. Moderate excess of turbid glairy brownish-pink fluid, probably containing inflammatory exudate, in the left knee-joint, with conspicuous hyperæmia of the synovia of the joint but no erosion of the articular cartilage. Slight excess of almost clear glairy brownish-pink fluid in the otherwise normal left hip-joint. Left femur, tibia, and fibula normal externally and on bisection, with no evidence of osteomyelitis. No abnormality of adductor or hamstring muscles of left thigh.

Hyperæmia of skin of inner aspect of left thigh above the middle, with several recent bullæ on the hyperæmic area. These bullæ were not observed during life and must be regarded as agonal. Several small pitted scars around both knees, and one on the back of the left thigh. No recent septic lesions on skin of thigh or elsewhere, except the bullæ already mentioned. No thrombosis of veins of left lower limb, although the femoral and popliteal vessels passed through purulent tissues.

Considerable inflammatory enlargement of left inguinal and iliac lymph-nodes. No hæmolytic staining of the lining of aorta or other blood-vessels. Swollen ill-defined malpighian bodies in bright purple-red pulp of slightly enlarged spleen. Blurred pattern in swollen suprarenal glands. A few purple-red radial streaks, but no abscesses, in cortex of kidneys. No pneumonia or abscesses in greatly congested lungs. Tonsils absent. Some cloudy swelling of myocardium; heart valves normal. Cyanosis of fingers. A well-nourished woman.

Microscopical and Bacteriological Examination

The purulent exudate in the left thigh contained very numerous streptococci, the left inguinal lymph-nodes were acutely inflamed, and severe parenchymatous degeneration was seen in the kidneys, excessive leucopoiesis in the bone-marrow, and slight centrilobular large-droplet fatty change in the liver.

Cultures from the affected muscles grew hæmolytic streptococci of group A, type 4, which were fully sensitive to penicillin, streptomycin, aureomycin, and chloramphenicol. Two cultures from the spleen were examined; one was sterile, but the other yielded a few colonies of streptococci.

SECOND CASE

A man, aged 33, by occupation a market trader, was admitted to Addenbrooke's Hospital on Oct. 27, 1952, complaining of severe pain in his left thigh. He said that the pain had begun the day before; it then prevented him from walking, and he had stayed in bed all day, sweating much.

On admission he was distressed and sweating, with temperature 103·2°F, pulse-rate 132, respirations 20 a minute. There was swelling and acute tenderness of the lower anterior part of the thigh, down to and including the patellar region, with erythema of the skin. Examination of his blood showed hæmoglobin 16·2 g. per 100 ml., leucocytes 23,000 per c.mm. (neutrophils 84% = 19,320 per c.mm., juvenile forms 6% = 1380 per c.mm., neutrophil myelocytes 0·5% = 115 per c.mm.).

Treatment and Course

The patient had been given an injection of penicillin before admission, and at 8 P.M. another was given (500,000 units). A blood-culture taken at 11.30 P.M. proved to be sterile. Further injections of penicillin 500,000 units were given three-hourly until his death on Oct. 29 (total dosage 6,000,000 units). On Oct. 28 he appeared very toxic and ill; his temperature was down to 98·4° F, but his pulse-rate remained 130.

Operation.—Under general anæsthesia an incision was made into the lateral aspect of his left thigh. Pus was observed coming from the under-surface of the rectus femoris muscle, and much of this muscle and the vastus lateralis muscle appeared necrotic: it did not bleed or contract. No pus was found around the femur, which looked healthy. Necrotic muscle was removed until healthy tissue appeared. Thin watery purulent fluid oozed from the cut surface of the necrotic muscle, but no gas was seen, nor were there any localised abscesses. The incision was closed with nylon sutures placed wide apart. The patient was now given aureomycin 250 mg. four-hourly, and later terramycin in an intravenous drip, but his condition steadily deteriorated; his pulse-rate rose to 200, and he died at 10.30 A.M. on Oct. 29, apparently of extreme toxæmia.

Necropsy Findings

Acute suppurative streptococcal myositis of left thigh. Thin pinkish-red purulent fluid exuded from the partially necrotic remnants of the left vastus lateralis and rectus femoris muscles. Similar exudate in fascial planes of the thigh from popliteal fossa almost to the groin. Surgical incision on lateral aspect of the left thigh. Adductor and hamstring muscles of left thigh almost normal in appearance. Left femur and hip- and knee-joints normal. Acute inflammatory swelling of left inguinal lymph-nodes. Slight general enlargement of lymph-nodes. Very soft purple-grey acute septic spleen. Pale red-brown myocardium and normal heart valves. Congestion and œdema of heavy dark purple-red lungs. Pale yellow patches on surface of swollen yellow-brown liver. The capsules stripped easily from the surfaces of the pale kidneys. No pyæmic abscesses found in any organ. A well-nourished young man.

Microscopical and Bacteriological Examination

Acute purulent myositis of the left thigh. Gram-positive cocci were abundant in some parts of the section, but many appeared degenerate and had lost their gram-positive staining; many had been phagocytosed by leucocytes. Severe acute inflammatory changes were present in the spleen, but no bacteria were seen in a gram-stained preparation. Numerous leucocytes were crowded in the sinusoids in some parts of the liver. Parenchymatous degeneration of kidneys. Congestion, hæmorrhages, and œdema of lungs.

Cultures of the purulent fluid from the left thigh muscles (operation specimen) gave a profuse growth of hæmolytic streptococci of group A, type 3, which were fully sensitive to penicillin, streptomycin, aureomycin, and chloramphenicol. Nose and throat swabs were taken on Oct. 31 from each of the four members of the patient's household. No hæmolytic streptococci were isolated from any of these swabs.

THIRD CASE

A housewife, aged 76, was admitted to Addenbrooke's Hospital on May 24, 1953. She was too ill and confused to give a history, but according to her relatives her illness had begun five days previously, when she had complained of pain in her face; for this she had applied a liniment. Next day she had pain in her left thigh and aching in all joints; a red patch "as big as a tennis ball" appeared on the outer aspect of her left thigh. Her nose was now swollen, and a scab formed on it. Two days later (two days before admission) she seemed very ill; her breathing was "very heavy" and her lips and cheeks looked blue, but she was said not to have been febrile. Malaise and general weakness continued, and the day before admission she fell down while walking to the lavatory.

On examination she was extremely ill, with signs of peripheral circulatory failure. Her nose, ears, and extremities were deeply cyanosed and her features pallid. Her temperature was 100°F and systolic blood-pressure 55 mm. Hg; the diastolic pressure could not be recorded; the pulse was of poor volume (rate 140). A scabbed lesion about 2 cm. in diameter was present on her nose. Her left leg was swollen, especially the thigh, which was very tender on its lateral aspect. All movements of this limb were very painful; it was held externally rotated. In view of the history of a fall, the possibility of a fracture of the neck of the left femur was considered, but the first need obviously was for treatment of the profound circulatory failure, which was thought possibly to be due to septicæmia, to pulmonary embolism, or to myocardial infarction. Treatment with intravenous infusions, 'Eucortone', penicillin (500,000 units), and nikethamide was, however, of no avail; and the patient died in coma about seven hours after admission.

Previous History

Rickets in childhood, and winter cough and "rheumatism" for years.

Necropsy Findings

Acute streptococcal myositis of the left thigh. Thin yellow-pink fluid exuded from the pale grey-pink cut surfaces of the vastus lateralis and adjacent muscles of the left thigh; there was one moderately well-defined abscess (1·5 cm. in diameter) containing thick creamy-yellow pus deep in the substance of the vastus lateralis muscle, with several smaller abscesses near it. No thrombosis or other abnormality of the veins of the left lower limb. Left femur, knee-joint, and hip-joint normal. Several superficial bullæ (largest 4 × 2 cm.) containing clear reddish fluid on skin of posterolateral aspects of left thigh just above the knee. No septic lesions of any kind on the rest of the skin of the left leg; the search particularly included the clefts between the toes. Rather soft and pale normal-sized spleen (125 g.). No hæmolytic staining of aorta or other blood-vessels. Moderately severe atheroma of coronary arteries, with narrowing and calcification. Rather flabby brownish-red myocardium. Heart valves functionally normal and devoid of vegetations. Congestion and bullous emphysema of rather small lungs. Patchy centrilobular congestion in pale liver. Blurred pattern on cut surfaces of suprarenal glands (acute inflammatory swelling). One dry crusted lesion (2 cm. in diameter) on the left side of the nose. Mild osteoarthritic changes and Heberden's nodes in both hands. A moderately well-nourished elderly woman.

Microscopical and Bacteriological Examination

The fluid which exuded from the affected muscles of the left thigh was found to be so rich in streptococci that it resembled a pure culture; sections of the muscle showed acute purulent myositis. Acute inflammatory changes were present in a left inguinal lymph-node. There was great engorgement of the sinusoids of the suprarenal glands, with focal cellular infiltration (mainly lymphocytic). No important abnormalities were seen in sections of spleen, liver, and kidney.

Cultures from the affected muscles of the left thigh gave a profuse growth of hæmolytic streptococci of group A, type 3, which were fully sensitive to penicillin, streptomycin, aureomycin, and chloramphenicol. Small numbers of the same kind of organism were found in the fluid from one of the bullæ near the left knee. A few hæmolytic streptococci were found in a swab taken at necropsy from the nares, but these were thought to be probably contaminants; no streptococci were found in an intranasal swab. Cultures from the spleen were sterile.

FOURTH CASE

A housewife, aged 72, complained of malaise on Feb. 27, 1956, and next day she stayed in bed, feeling shivery. On Feb. 29 she sent for her doctor because she had a pain in her left upper limb; this pain was in the region of the shoulder and scapular region, and the patient regarded it as rheumatism, saying that she had had a lot of pain in her right shoulder for several months, but that it was now better. Some years previously she had been treated for a rheumatic swelling in one hand.

On examination her temperature was 101·2°F and pulse-rate 80; her left shoulder was not hot or swollen, but there was an irregularly shaped patch of erythema inside the left elbow. The patient said that she had had a similar red patch on one arm a few weeks before.

Course and Treatment

Despite analgesics and a barbiturate tablet the pain in the left arm disturbed her sleep, and next morning (March 1) there was some swelling of the upper part of the arm, which was tender to touch and painful on movement. She was transferred to a nursing-home because nursing facilities at home were inadequate; on admission at about 11 A.M. her temperature was 99·2°F, pulse-rate 80, and respirations 28. In the evening her arm looked and felt the same, except that the patch of erythema was much paler. Her colour was good, and she looked sleepy and quiet. Nevertheless her nurse thought she appeared more ill than her temperature (99°F), pulse-rate (84), and respirations (24) suggested. That night the patient slept at first, but at 2 A.M. her condition was very poor, and she seemed to have difficulty in swallowing; her temperature now was 103°F, pulse-rate 106, and respirations 38. Her condition continued to deteriorate, and about 4.30 A.M. she became unconscious, with feeble pulse, and shallow respirations. Nikethamide, oxygen, intramuscular penicillin (600,000 units), and intravenous saline solution and glucose did not revive her, and she died at 6.25 A.M. on March 2.

Necropsy Findings

Acute streptococcal myositis of the left triceps brachii. Swelling of left upper arm, with an area of brawny œdema on its posterior surface. Numerous ill-defined abscesses in the pale-brown triceps muscle; pus in intermuscular septa and adjacent to the humerus. No evidence of osteomyelitis in humerus after longitudinal bisection. Left shoulder-joint and elbow-joint normal. One superficial scratch (less than 1 cm. long) on the skin of the metacarpo-phalangeal joint of left thumb; this appeared to be several days old and did not look inflamed. Slightly enlarged and acutely inflamed lymph-nodes in left axilla. No thrombus in normal left brachial vein and artery. No hæmolytic staining of aorta or other blood-vessels. Heart valves normal and free from vegetations; myocardium brown and flabby. Diffluent pulp in small soft purple spleen. Moderately severe congestion and œdema of lower and posterior parts of lungs. Cloudy swelling of cortex of kidneys, with a few patches of hyperæmia just under the capsule. No pyæmic abscesses in the kidneys or in any other organs. Scars of old tonsillectomy and partial thyroidectomy operations; thyroid gland represented by small remnants of lateral lobes only. A well-nourished elderly woman.

Microscopical and Bacteriological Examination

Smears from the pus in the left triceps muscle showed numerous gram-positive cocci in chains, and in sections of the muscle the picture was that of acute purulent myositis. Acute inflammatory changes were seen in the left axillary lymph-nodes and the spleen; severe congestion, œdema, and intra-alveolar hæmorrhage in the lower lobe of the left lung; large-

droplet fatty change of moderate degree in the liver; severe degenerative changes in the cortex of the kidneys; and benign hypertensive changes of moderate degree in the arteries and arterioles of the kidneys and suprarenal glands.

Cultures from the pus in the triceps muscle gave a profuse growth of hæmolytic streptococci of group A, type 12, which were fully sensitive to penicillin, streptomycin, aureomycin, and chloramphenicol. Cultures from the spleen were sterile.

Discussion

These four examples of spontaneous streptococcal myositis were acute febrile illnesses associated with pain and swelling in the muscles of a limb, leading to profound toxæmia with rapid feeble pulse, circulatory collapse, and death. The patient may be young or old: the pain may begin before or shortly after the constitutional disturbances. In none of our four patients was the existence of septicæmia proved, unless the few colonies of streptococci obtained from one of the two cultures of the spleen of case 1 at necropsy is held to provide such proof. In none of these cases, however, was blood-culture undertaken before antibiotic therapy was instituted, and in all probability general dissemination would have taken place before death if the patients had not been given such therapy. Nevertheless, the myositis cannot reasonably be regarded as merely an incident in the course of a streptococcal septicæmia.

Published reports of such cases as these are few, if one excludes the tropical cases already mentioned (Manson-Bahr 1954).

Payne (1881) described a case of acute myositis of the thigh of a woman aged 33; but, since the illness began during the puerperium and there is no note of the state of the veins at necropsy, the possibility of septic thrombophlebitis cannot be excluded.

Clark (1887) described a more definite case in a man aged 29, but neither in this case nor in that of Payne were the causal organisms identified; so they may not have been streptococci.

Abram (1904) recognised streptococci as a cause of suppurative myositis and described two cases involving a pectoralis major muscle; these patients both recovered after surgical incision.

Abrami and Worms (1930) described two cases, one involving the muscles of the shoulder region of a man aged 30, the other the thigh of a man aged 38, who also had streptococcal arthritis of a knee-joint. In the former case streptococci were cultured from the blood. These workers remark that such cases are rare and that " la myosite streptococcémique suraigue . . . représente une entité nouvelle ".

Traumatic streptococcal myositis, usually due to anærobic streptococci, was described by MacLennan (1943a and b, 1944), but this is in many ways different from the spontaneous myositis due to aerobic streptococci in the present cases. The following case more closely resembles those of MacLennan, but the infecting organisms were aerobic streptococci of group A.

FIFTH CASE

A man, aged 75, sustained a fracture of the neck of his right femur on Sept. 23, 1952, and at operation next day the femoral head was removed and a Judet prosthesis fitted. Prophylactic penicillin therapy was given from the first to the tenth day after operation (total dosage 13,500,000 units). The patient was found to have purulent bronchitis and emphysema. On the sixth and seventh postoperative days there was a very slight rise of temperature (maximum 99°F); otherwise he was apyrexial. He was discharged on Oct. 13. On Nov. 15 he was found dead, lying on the floor near the bed at his home.

Necropsy Findings

The right hip-joint contained milky-grey pus, and a large abscess cavity (12 × 14 cm.) was present in the right buttock. The abscess communicated with the hip-joint through a large aperture in the posterior part of the capsule. The arthroplasty incision was completely healed, and there was no external evidence of infection. Except for some acute bronchitis and bronchiolitis in the lower lobes of the lungs, no important abnormalities were found elsewhere in the body, and death was attributed to the arthritis and buttock abscess.

Bacteriology

The pus contained hæmolytic streptococci of group A, type 11/27/44. Cultures from the spleen yielded a profuse growth of the same organisms; these were fully sensitive to penicillin, streptomycin, aureomycin, and chloramphenicol.

The streptococci may have gained access to the hip-joint at the operation and been suppressed but not exterminated by the subsequent antibiotic therapy, only to multiply when this was stopped. The possibility of hæmatogenous infection of a hæmatoma cannot, however, be excluded.

In the cases of spontaneous myositis (cases 1–4) the infection probably reached the muscle via the blood-stream, because in none of the cases was there any history of a recent penetrating wound or of any intramuscular injection. The portal of entry of the infection into the body remains obscure.

The possibility of acute streptococcal myositis should be considered if a febrile patient complains of acute pain and tenderness of the proximal part of one limb, and on examination is found to have definite swelling of a muscular part of the limb, perhaps accompanied by a patch of skin erythema which may not immediately overlie the site of greatest pain and swelling.

Unfamiliarity with the condition is the greatest obstacle to its diagnosis.

Acute thrombophlebitis may be suspected, but the absence of œdema of the distal part of the limb and the absence of engorgement of the superficial veins speak against it. In *acute osteomyelitis* the swelling is usually nearer to the end of a long bone, and the patient is likely to be younger. The distinction between myositis and cellulitis may be difficult but is probably not of great practical importance. Sudden development of profound toxæmia is one of the distinctive features of myositis. Failure to recognise the onset of this toxæmia may have serious consequences. The patient's temperature is unreliable as an index of his progress because it may fall as the toxæmia develops, and this may erroneously suggest improvement. The continued rise in the pulse-rate and the general deterioration of the patient's condition should, however, reveal the true state of affairs.

Streptococcal infections are now apt to be regarded too lightly. As the cases here reported illustrate, the dangers of such infections are by no means past, and early diagnosis is of great importance. Streptococci are sensitive to most antibiotics and very rarely become resistant; consequently antibiotic therapy may be expected to have excellent results if it is instituted early. On the other hand, even the most massive antibiotic therapy may prove unavailing when severe toxæmia has already developed.

Summary

Acute streptococcal myositis was fatal in 4 patients The thigh muscles were involved in 3 and the triceps brachii in the other.

The portal of entry of the streptococci was not established.

This infection can be fulminating; and early diagnosis and early antibiotic therapy are essential.

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DERMATITIS CAUSED BY PENICILLIN IN MILK

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THE incidence of sensitivity to penicillin is probably about 5% for the general population and 12–15% for those engaged in its manufacture or who have multiple allergies (Brown 1948, Boger et al. 1953, Feinberg and Feinberg 1956, Frome 1957).

The first cases of contact dermatitis due to penicillin were in people exposed during its manufacture. Many cases were later seen in nurses and in patients who had been treated with penicillin in contact with the skin for long periods (Pyle and Rattner 1944, Michie and Bailie 1945, Vickers 1946).

Since the introduction of machine milking, the incidence of mastitis in cows has increased, and the common practice among herdsmen is to inject 100,000 units of procaine penicillin into the teat of the infected quarter. 70% of cases are due to *Streptococcus agalactiæ*—an organism highly sensitive to penicillin—and the infection rapidly subsides (Milton 1950). As a result of this treatment, milk may contain penicillin, and this has already given rise to anxiety in the United States (McLean 1956, Welch 1957). If patients previously sensitised to penicillin by local application drink milk containing penicillin, dermatitis may develop and persist indefinitely if its true nature is not recognised.

We have recently seen two patients in whom penicillin in milk seems to have been the cause of dermatitis.

Case-reports

Case 1.—A woman, aged 55, gave a long history of skin trouble, starting with eczema in infancy. At the age of 20 dermatitis of the neck developed owing to contact with brown dyed fur. When aged 33, she had dermatitis of the suspender areas.

At the age of 45 a rash then developed on her ears after contact with a pig with scaling ears; treatment with penicillin resulted in severe dermatitis of the ears, and the rash spread to the face and neck.

At the age of 49, a rash had developed on her hands while she was working in a plant nursery. Allergy tests, in hospital, were all negative. After fourteen weeks in hospital she improved, but thereafter she had recurrent attacks of dermatitis affecting particularly the face and hands.

A further attack started in April, 1957, (when the patient was aged 55) and she had an acute exacerbation two days before coming to the outpatient department in August. She then had acute dermatitis, with erythema and weeping, of the whole of her face, neck, and the backs of the hands and forearms.

Investigation

The patient was admitted to hospital with a diagnosis of acute contact dermatitis. The condition slowly improved. She was patch-tested to the following suspected contacts: penicillin 200,000 units per ml., 2% nickel sulphate, English yew, tulip, Douglas fir, Lawson cypress, macrocarpa cypress, chrysanthemum, cineraria, lupin, tomato, strawberry leaf, raspberry leaf, carnation, antirrhinum, phlox, wallflower, privet, ivy, sweet-william, foxglove, and primula. She gave strongly positive reactions to penicillin, primula, and nickel sulphate. Other patches were negative.

A more detailed history revealed that the patient had lived on farms for many years. In 1956, when she had her own cow, which had not had penicillin, she was well, but when the cow stopped lactating and she had fresh bulked milk, probably containing penicillin, she had a relapse. Her previous attacks had been associated with drinking about a litre of fresh bulked farm milk daily. She improved when away from the farm.

Desensitisation

It was decided to desensitise the patient to penicillin. She gave no reaction to 2 units, but 4 units intramuscularly produced an exacerbation of the dermatitis on the previously affected areas. The dose was then reduced to 1 unit, and to avoid penicillin-contaminated milk she was given goat's milk. On these small doses of penicillin she had much irritation, and some of the injections were followed by nausea. With perseverance, however, the daily dose was increased so that she now tolerates 1,000,000 units, and the dermatitis has cleared. She has returned to drinking cow's milk with no ill-effects.

Analysis of fresh milk from the farm where she lived showed a penicillin content of 4 units per ml.

Case 2.—A man, aged 44, was admitted to hospital on Sept. 27, 1957. He has a small mixed farm, with 14 cows milked by machine. Ten days before admission he had an attack of lumbago. Five days later a rash developed round the genital and pubic region, which was treated with 'Caladryl'. The day before admission the rash became generalised and was accompanied by fever (101° F), palpable painful glands in the groins and axillæ, and swelling of the knees and ankles. Twenty years ago he had a transient rash on the arms and abdomen, and eighteen months ago a similar rash on the back.

On examination he had severe erythema of the whole skin. On the trunk and thighs there were small tightly packed vesicles, many of which contained turbid fluid. There was much swelling of the lower legs, and the lymph-glands in the neck, axillæ, and groins were palpable and tender.

Acute epidermal sensitisation, probably due to a drug, was diagnosed. On being questioned further, the patient said that he had been giving his cows penicillin for mastitis for two years. He had started to treat one with procaine penicillin (100,000 units into each quarter) ten days previously. Milk from this cow had been added to the rest of the farm milk, which he had been drinking.

He was treated with prednisolone, because the reaction was severe; it rapidly subsided. Patch tests were positive to procaine penicillin 100,000 units per ml. and negative to caladryl.

Discussion

Welch et al. (1955) found penicillin, in concentrations of 0·003–0·08 units per ml., in 11·6% of 474 samples of milk examined from sixteen States in America. The maximum quantity was thus about 20 units per glass. Moreover, penicillin could be detected in the milk six days after treatment, though most had been excreted after three days.

In a later survey the same workers (Welch et al. 1956) found penicillin in a concentration of 0·003–0·550 units per ml. of milk in 5·9% of 170 samples. The American

Food and Drug administration has ruled that milk from any cow which has been treated with penicillin should be discarded for seventy-two hours. It seems, however, that this order is not universally observed, and sometimes penicillin may even have been added to milk as a preservative. Penicillin in milk is well recognised as a cause of urticaria in America (Welch 1957), but we have been unable to find any records of its being responsible for the reactivation of dermatitis in patients previously sensitised.

In Britain there is a rather indefinite ruling that milk from infected cattle shall not be distributed. Since mastitis can often be diagnosed early and penicillin produces in most cases a rapid cure within hours, most of the milk from mildly infected cattle is distributed in the normal way.

Berridge (1956) found over 0·01 units of penicillin per ml. of bulked milk in 4·9–47% of a large number of samples from eight districts in England and Wales. In some samples the concentration of penicillin reached 0·8 units per ml. of milk. For single producers, 0·036 units or more per ml. was found in 1·4–4·8% of samples from seven districts, and 0·01 units or more in 4·2–18·5% of samples. There seemed to be no seasonal variation.

Naturally those living on dairy farms, like the two patients described here, will be more liable to a high penicillin intake than the general population, which benefits from more extended bulking with consequent dilution of the penicillin content. Our first patient drank nearly a litre of milk daily. As milk from her farm contained 4 units of penicillin per ml. she may have ingested 4000 units of penicillin daily. She was sensitive to 4 units of crystalline penicillin G intramuscularly.

The blood content after injection of 4 units would be about 0·000013 units per ml. (Florey 1952). Bierlin (1956) described a penicillin-sensitive patient who reacted severely to an injection of 0·000003 units of the drug. Salk poliomyelitis vaccine contains 0·5 units of penicillin per ml. (Siegal 1955) and has produced reactions observed in this hospital and in the United States (Clyde 1956). Carter and Cope (1954) reported a severe constitutional reaction to the topical application of penicillin eye ointment, and Madali (1954) reported a severe reaction to a penicillin lozenge one minute after it had been placed in the mouth.

The incrimination of penicillin is beyond doubt in both the cases reported here. Many chronic skin lesions of obscure origin may in fact be kept active by the daily ingestion of penicillin-contaminated milk. It seems that the penicillin content of bulked milk is so low as to be innocuous to normal persons, but not to the sensitive.

The number of persons sensitive to penicillin increases with the more widespread use of the drug. Accordingly it is important that this country should adopt the American ruling prohibiting the distribution of milk for seventy-two hours after the treatment of mastitis.

Summary

Two cases are reported of allergic dermatitis due to penicillin in milk from cows treated for mastitis.

One sample of milk tested contained 4 units of penicillin per ml.

It is suggested that the American ruling prohibiting the sale of milk from cattle for seventy-two hours after the last injection of penicillin should be adopted in Britain.

We thank Dr. W. H. H. Jebb and Mr. A. H. Tomlinson, of the Public Health Laboratory, Oxford, for the estimations of penicillin in milk.

References at foot of next column

FATE OF ORLON AORTIC IMPLANT IN MAN

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SINCE successful aortic grafting with cloth tubes was first reported (Blakemore and Voorhees 1954, Shumacker and King 1954) this method has proved its worth in many patients. So far no observations seem to have been made on the way in which such material is finally accommodated in the human aorta ; most of the published data concern experimental operations on the dog, and specimens recovered from patients who died soon after operation. We describe here our findings in a patient who died two and a quarter years after the insertion of an abdominal aortic graft of ' Orlon ' cloth.

Case-report

A man, aged 63, with pulmonary tuberculosis began to have nausea and abdominal pain soon after the first administration of streptomycin and *p*-aminosalicylic acid. Examination by Dr. G. Shneerson revealed an abdominal mass which he diagnosed as an aortic aneurysm. The pain increased, and on Feb. 16, 1955, we explored the abdomen and resected a large aneurysm which involved the aorta from 3–4 cm. below the renal arteries to the first part of the common iliac arteries. This gap was restored by means of a graft of orlon cloth previously prepared in the form of a bifurcation. The graft fitted well at the upper end, but the iliac branches were rather narrower than the corresponding ends of the patient's somewhat dilated iliac arteries; the cuffs of the branches were turned down, reducing this disproportion but requiring the suture of only a single layer of cloth at the two lower anastomoses, instead of the double fold preferred. The patient recovered well and experienced no further pain; but he was still unable to tolerate chemotherapy, and the tuberculosis progressed. On May 27, 1957, two and a quarter years after the operation, he died during a hæmoptysis.

Postmortem Appearance

The external appearance of the specimen recovered at necropsy suggested that it consisted simply of most of the abdominal aorta and the first parts of the common iliac arteries, with the stumps of the cœliac, mesenteric and renal arteries and the related parts of the corresponding veins (fig. 1). The upper cut end was 2·5 cm. (1 in.) above the cœliac axis; the right common iliac artery was about 6 cm. long, while the left was about 3 cm. long and was noticeably wider than the right. When the specimen was cut down its left lateral border and

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opened out, the orlon graft was immediately revealed, the weave of the fabric being only partly obscured by patches of fibrin. The graft had replaced the excised arteries from a line 4 cm. below the renal arteries down to lines 1·5 cm. beyond the origins of the common iliac arteries. There was considerable atheroma, especially of the common iliac arteries; the right was of about normal calibre, but the left was dilated and measured 2 × 1 cm. in cross-section. The following striking features call for comment:

Fig. 1—Specimen from front. Dark rods show positions of inferior vena cava and right and left renal veins.

(1) Fibrin had been deposited on the internal aspect of the orlon only in patches. The patches were irregular in outline and did not exceed 0·5 mm. in thickness, and large areas of the orlon appeared completely bare.

(2) The external aspect of the orlon was not attached to the surrounding tissues except at the anastomoses and down the sides, where there were seams joining the anterior and posterior halves of the graft. At other places the orlon either was absolutely loose or could be easily detached from the surrounding tissues, leaving an imprint of its mesh on the tissue surface with which it had been in contact.

(3) There were transverse wrinkles in the orlon at some places—notably near the upper anastomosis posteriorly, a little lower down anteriorly, and just above the iliac anastomoses. In the last-named situation the wrinkles made a much larger proportional reduction of the lumen than in the aorta, but there was no evidence that the wrinkles had affected the site or increased the likelihood of fibrin formation.

Fig. 2—Complete specimen opened out after cutting down its left border. Note detachment of orlon (at right lower corner).

(4) At the right side of the graft, near its upper end, a free edge of the orlon, showing the dentate outline caused by pinking shears, had been inadvertently turned in and was protruding into the lumen. Here again there was no increase of fibrin formation.

(5) The tissue around the graft was dense pale grey connective tissue, for the most part measuring less than 1·5 mm. in thickness.

These features can be observed in figs. 2 and 3.

Strips of the orlon and related connective tissue were taken from the front and back of the graft, including one of the seams. Sections were prepared for histological examination, from which the following points emerge:

(1) The tissue covering the orlon exteriorly is dense collagenous fibrous tissue, almost avascular, with few fibrocytes and very few, if any, elastic fibres. A thin layer of fibrin-like material is interposed at some places between the fibrous tissue and the orlon, but there is no other indication that the orlon has any irritative or "productive" effect on contiguous tissues. The dense connective tissue around the graft was probably formed by organisation of fibrin laid down at the time of insertion of the graft or soon after.

(2) There is no colonisation or infiltration of the orlon by fibroblasts or histiocytes. The only place where anything resembling this was observed was on the exposed aspect of the lateral seams; but it is not truly a matter of infiltration but of enclosure.

(3) Very little foreign-body giant-cell reaction was observed. Again the seams are the exception, and again appearances are deceptive, for the reaction is in fact most pronounced in relation to the thread used in stitching the seams. This thread, which was nylon, can be distinguished partly by its orientation and partly by its being more strongly anisotropic than the orlon.

(4) The fibrin adhering in places to the orlon has in its meshes only polymorphs and a few red cells. There is no sign of endothelialisation.

Comment

Very little is known about the long-term results of putting plastic grafts into the human body; but those that survive the operation and its immediate complications appear to do very well. Experimental operations in dogs (Voorhees et al. 1952) have indicated that such grafts become permeated, lined, and surrounded by fibrous tissue. Hufnagel (1955), dealing with orlon grafts, says:

Fig. 3—Interior of orlon graft and anastomosis with abdominal aorta. Note mesh of cloth, obscured by patches of fibrin (e.g., top right).

"The inner surface becomes covered with fibrinoid material . . . gradually islands of endothelial like cells appear on the surface; this process then continues with coalescence of these areas to form a layer within the orlon, and a fibrous layer outside it. . . . Some fibres appear to grow through the spaces in the orlon cloth although these are quite fine and tenuous in character."

In the present case a very different condition is found. Scar tissue has been formed only *outside* the graft; the cloth itself seems to have been almost inert to the host cells and tissues. "Foreign body reaction" towards the fabric has been negligible, nor has the orlon aroused much fibrin formation, yet there has been no leakage through any part of it. Wrinkles and other faults in the preparation and insertion of the graft do not seem to have mattered. In some ways this inert behaviour reflects that of the arterial homograft in man. Rob (1954) reported only very incomplete active invasion and practically no

lining by host cells in several homografts in man exhibited some months after implantation.

The findings in this case are so surprising that some peculiarity of the patient or his treatment may be suspected. This question can be settled by future findings in other patients with orlon grafts or with grafts of another cloth such as ' Terylene '.

We are indebted to Dr. John Taubman for recovering the graft at necropsy.

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FULMINATING BERIBERI

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BERIBERI is very rare in Great Britain; only 13 deaths from it were recorded in this country over the five-year period 1949–53. Fulminating beriberi is almost unknown in Great Britain.

Yudkin (1938) described a young Indian who developed anorexia, dyspnœa, malaise, œdema, palpitations, and tachycardia after living in London for eight months on a diet of polished rice. This patient, and others with cardiovascular disease, responded to large doses of aneurine (vitamin B_1) (Price 1938, Jones and Bramwell 1939, Ungley 1939, Konstam and Sinclair 1940, Bates 1941, Paulley and Aitken 1944, Thomson and Keay 1952). Fatal cases were reported by Wood (1939), and by Allibone and Baar (1946).

Only in the past fifteen years has it been generally recognised that beriberi may present not only as the well-known syndrome of œdema, heart-failure, and peripheral neuropathy, but also with cerebral manifestations—the long-recognised syndromes of Wernicke's encephalopathy and Korsakow psychosis. We describe here a case of fulminating beriberi showing all five possible manifestations of aneurine deficiency—namely, peripheral neuropathy, heart-failure and œdema, Wernicke's encephalopathy, and Korsakow psychosis —a combination not, we believe, previously reported in Britain.

Case-report

A woman, aged 55, was admitted to the neurosurgical department of the Royal Northern Hospital on July 27, 1955, for investigation of her complaint of weakness of the legs. She had been quite well until May 28, when she felt faint, and collapsed on the floor and hit her head. After resting in bed for a month she was well apart from an occasional bout of vomiting, headache, and giddiness; but when she tried to stand again her legs collapsed under her. Her relations noticed that she was sometimes drowsy and confused. Her doctor found a motor ataxia and bilateral nystagmus, suspected a subdural hæmatoma or a cerebellar tumour, and referred her for a neurosurgical opinion.

The patient was thin, weighing 7 st. There was some loss of memory for recent events including the actual fall. She walked with difficulty. All her limbs were wasted; and there was fasciculation of the muscles, but their tone and power were normal except for bilateral weakness of ankle dorsiflexion. All tendon reflexes were absent, but the plantar responses were normal. No abnormal physical signs were found in the sensory system, the cranial nerves, or any other system of the body. She had had no other serious illnesses. She lived alone and did part-time work as a railway toilet attendant. Both she and her relations maintained that her diet was full, and that she drank an occasional glass of beer only.

Investigations

Peripheral neuropathy was diagnosed, and the underlying cause was investigated. Radiographs of the skull and chest, the blood-count, and the cerebrospinal fluid were normal. The Wassermann and Kahn reactions were negative. There was histamine-fast achlorhydria. In the sternal marrow there was no evidence of megaloblastic erythropoiesis. Electromyography of the arm and leg muscles showed fibrillation with some decrease in the pattern of motor activity on voluntary movement. Conduction in all the long nerves in the arms and legs was normal. These findings supported the diagnosis of peripheral neuropathy.

Course

With the aid of physiotherapy the patient's walking improved, but on Aug. 21 she suddenly became unwell, losing her appetite and vomiting her meals. By Aug. 23 she was apathetic and apprehensive, her tongue was smooth and pale, and her calves were very tender. Next day she became frightened, disoriented, and confused, with delirium and hallucinations; she lay listlessly curled up in bed, and refused to eat. Retention of urine developed and she had to be catheterised.

On the morning of Aug. 25 the patient rapidly lapsed into stupor. She was motionless, and sacral and ankle bedsores had developed. She could not move her eyes downwards or laterally, and there was divergent strabismus with disconjugate wandering and failure of convergence. Her fundi were normal. There was mild intention tremor. Wernicke's encephalopathy with peripheral neuropathy, due to avitaminosis, was diagnosed. She was at once treated with vitamins B and C by injection of 7 ml. high-potency ' Parentrovite ' * twice daily for seven days, followed by the maintenance preparation; in addition cyanocobalamin (vitamin B_{12}) was injected—1 mg. daily at first, and then 100 μg. daily.

Next day ascites appeared, with œdema of the sacrum and legs, tachycardia, and a raised jugular venous pressure; but she was more alert and could conduct a simple conversation. The diagnosis was now established as beriberi. She was given a high-calorie and high-protein diet through a Ryle's tube.

Progress Under Treatment

The signs of heart-failure had disappeared by Aug. 30, when convergence and downward movement of the eyes had recovered. The paralysis of lateral movement lasted for two days only, and was then followed by nystagmus. This was at first produced by small deviations of the eyes, and then gradually improved to appear only at the extreme range of lateral movement. There was transient right facial paresis and ptosis on Aug. 28. Soon the patient became cheerful and voluble and began to read the newspapers again, but her amnesia for the recent past was complete and she confabulated freely (Korsakow's psychosis). She continued to have delusions and hallucinations, but the vomiting stopped; she took a large solid diet, and gradually walked unaided.

On Oct. 8 she had numbness, pins and needles, and cramp in the hands, and a few days later similar sensations in her legs. Her calves were only slightly tender. On Nov. 3 her ankles became swollen again, and œdema increased in the following week. On Nov. 11 she became suddenly breathless, with precordial pain and anxiety. The pulse-rate was 120 a minute. The apex-beat was six inches from the midline in the seventh intercostal space. The jugular venous pulse was at the angle of the jaw and the abdomen swollen. Treatment

* Parentrovite (high potency) contains in each 7 ml. Aneurine hydrochloride 250 mg., nicotinamide 160 mg., riboflavine 4 mg., calcium pantothenate 5 mg., pyridoxine hydrochloride 50 mg., and ascorbic acid 500 mg. The maintenance preparation contains 100 mg. of aneurine, but is otherwise identical.

with oxygen and intravenous morphine and aminophylline brought about rapid improvement. By next morning the pulse-rate was 80 a minute, the size of the heart and the venous presssure were normal, and there was neither œdema nor ascites.

Neither then nor during the previous episode of heart-failure did the electrocardiogram show any specific changes. In view of the histamine-fast achlorhydria, a search was made in the alimentary tract for the cause of the aneurine deficiency. The glucose-tolerance test and the content of fats and nitrogen in the fæces were normal. A barium-meal and follow-through examination showed gastric stasis only; but gastroscopy revealed advanced gastric atrophy.

Condition on Discharge

The patient was discharged from hospital on Nov. 22, on maintenance injections of vitamin B_{12} and parentrovite. Her condition on discharge, after three months' vitamin therapy, was similar to that on admission. She had a mild Korsakow syndrome, slight lateral nystagmus, intention tremor, unsteady gait, and signs of peripheral neuropathy in the legs. When she was seen as an outpatient a month later she was able to walk without a stick, the reflexes in the upper limbs had returned, but otherwise her condition was unchanged.

Discussion

Wernicke's first case of encephalopathy was in a young seamstress in whom pyloric stenosis developed after she had taken vitriol.

Having vomited persistently for five weeks she was admitted to hospital drowsy and apathetic, with ataxia and failing vision. There developed slight right facial palsy, ptosis, nystagmus in all directions, convergent strabismus, and paralysis of horizontal movements of both eyes. She continued to vomit, and over the next few days she became disoriented and had fever and tachycardia. She lapsed into coma, and papillœdema and flame-shaped hæmorrhages developed in both eyes. She died ten weeks after swallowing the acid.

Recent reviews, such as those of Campbell and Russell (1941), de Wardener and Lennox (1947) and Cruikshank (1950) have added little to this description.

The premonitory anorexia, nausea, and vomiting are followed by eye symptoms (failing vision, photophobia, diplopia), insomnia, and giddiness. All patients have some eye signs (nystagmus, ocular palsies, disconjugate wandering, strabismus, papillœdema, hæmorrhages, and ptosis). Often other cranial nerves are involved or the pyramidal system is affected. Most patients have mental changes (apprehension, apathy or excitement, loss of memory for recent events, disorientation in time and space, hallucinations, and confabulation). It was just such a combination of polyneuritis and disturbances of emotion, memory and orientation, that Korsakow described in 1887 in patients with toxæmia, usually in alcoholics.

Pathology

The lesions found at necropsy by Wernicke in his 3 cases have often been shown since. The typical features have been summarised by Cruikshank (1950):

"A selective distribution of focal lesions throughout the grey matter of the brain, consisting of hyperæmia sometimes accompanied by small hæmorrhages, endothelial and mesenchymal vascular proliferation, and a varying degree of glial proliferation, without inflammatory infiltration and with relatively slight evidence of damage to nerve-cells. The localisation of the lesions was characteristic; they were constant and most marked in the corpora mamillaria and less constant in the other hypothalamic nuclei. In the mid-brain they were frequently seen in the periaqueductal grey matter, involving the oculomotor nuclei. Nothing characteristic was found in the cerebral cortex."

Wernicke (1881) considered these lesions inflammatory, allied to poliomyelitis, and he called the disease "die akute hämorrhagische polioencephalitis superior". 2 of his patients were chronic alcoholics, and most authors for the next half-century and many current textbooks describe chronic alcoholism as the invariable cause, as suggested by the title "encephalopathia alcoholica" (Bender 1934). Neuberger (1936) was the first to describe a series of non-alcoholic patients with Wernicke's syndrome, though Tanaka (1934) had already shown, both clinically and histologically, that *kakke*, the so-called breast-milk intoxication, or infantile beriberi, is identical with Wernicke's encephalopathy.

Wechsler (1932) suggested a deficiency of aneurine as the cause of Wernicke's encephalopathy, and Alexander (1940) showed that in animals deficient in aneurine, brain lesions develop identical with those of this disease.

Dunlop, cited by Campbell and Russell (1941), cured a woman with Wernicke's encephalopathy by injecting aneurine. Joliffe et al. (1941) tried various treatments on 27 patients with the diagnosis of Wernicke's encephalopathy. Of 13 given intramuscular aneurine, 8 survived; whereas of 14 treated without parenteral aneurine, only 4 survived. de Wardener and Lennox (1947) reported on 52 patients they had seen as prisoners-of-war in Singapore in 1942, and having read of Dunlop's success in the review of Campbell and Russell (1941) were able to cure many of them even with the small stocks of thiamine at their disposal. The encephalopathy in these prisoners-of-war arose at a time of acute thiamine deficiency and of the development of other forms of beriberi.

Other signs of aneurine deficiency were reported in 72 of the 106 cases in four series (Campbell and Russell 1941, Joliffe et al. 1941, de Wardener and Lennox 1947, Cruikshank 1950). The deduction of these authors that the Wernicke syndrome is "cerebral beriberi" seems inescapable. The principal objection of Campbell and Russell (1941) to the deficiency hypothesis (as opposed to Neuberger's toxæmia theory) was the absence of reports of cerebral involvement in accounts of beriberi (e.g., Bentley 1893). Cruikshank (1950), however, was able to find accounts of clinical manifestations (especially ocular) and pathological features in the older reports on beriberi, as well as in Tanaka's (1943) review of infantile beriberi.

It is now recognised that Wernicke's encephalopathy is caused by an acute deficiency of aneurine from: (*a*) insufficient intake (undernutrition or malnutrition); (*b*) failure of absorption (alimentary disease or any condition associated with vomiting); (*c*) impaired utilisation (liver disease); or (*d*) excess demand for the vitamin (pregnancy and lactation, exercise, and toxic and febrile states).

In 240 cases reported by 25 authors the ætiological factors were:

	No. of cases
Deficient intake (excluding alcholism)	93
Alcoholism	82
Alimentary disorders:	
Carcinoma	26
Protracted vomiting	22
Gastric atrophy	17

Gastric atrophy, the most likely causal factor in our patient, was present in 17 (7%) of the 240 cases. Only a third of the patients were alcoholics.

Diet and Vitamins

Wernicke's syndrome does not develop in pigeons given either a vitamin-free diet or aneurine and a diet lacking the other vitamins. Only when aneurine-deficient pigeons are liberally supplied with other vitamins does the disease develop. Furthermore, beriberi does not develop in men who are starved, for there must be a minimum carbohydrate content to the diet.

Aneurine diphosphate (cocarboxylase) is needed in the metabolism of carbohydrate. The daily human requirement

FATE OF 240 REPORTED CASES (1881–1951) OF WERNICKE'S ENCEPHALOPATHY IN RELATION TO TREATMENT WITH PARENTERAL ANEURINE

—	Survived	Died	Total
Treated ..	58 (*69%*)	26 (*31%*)	84
Untreated ..	10 (*6%*)	146 (*94%*)	156
All	68 (*28%*)	172 (*72%*)	240

is not an absolute figure but varies with the carbohydrate content of the food, being about 2 mg. for an ordinary 3000 calorie diet. This vitamin content in mg. of aneurine (A) can be expressed as a ratio per thousand non-fat calories (N.F.C.). Studies of human aneurine deficiency, both experimental and natural, show that where this ratio A./N.F.C. falls below 0·3, symptoms of deficiency appear (Williams and Spies 1938).

30,000 men were suddenly changed from a normal to an aneurine-deficient rice diet when Singapore was captured in 1942. Wernicke's encephalopathy appeared among British prisoners after six weeks, when the A./N.F.C. ratio was about 0·194. Of de Wardener and Lennox's 52 cases, 45 had dysentery or diarrhœa as a precipitating factor. With improvement in the diet there were no further cases. In the months before the liberation in August, 1945, the ratio A./N.F.C. was just above the critical 0·3. After the liberation the diet was suddenly supplemented by rice and protein, the A./N.F.C. fell to 0·204, and a beriberi outbreak appeared within fourteen days (Pantridge 1946).

Barrie (1947) was the first to emphasise the danger of the routine hospital diet (? high calorie, low aneurine) to patients with aneurine deficiency. He reported that 3 patients who had vomited for months or years from gastric disease died of Wernicke's encephalopathy after being admitted to hospital. Perhaps our own patient is another example of a few weeks of a hospital diet suddenly increasing the denominator, and thus lowering the ratio A./N.F.C., and precipitating the acute deficiency state of Wernicke's encephalopathy.

It is not clearly understood how gastric atrophy produces the secondary deficiency of aneurine, a vitamin absorbed in the intestines; but it is known that achlorhydria is associated with an altered intestinal bacterial flora, which may interfere with the absorption of dietary vitamins.

Treatment

Wernick's encephalopathy, or indeed any case of fulminating beriberi, is best treated by immediate administration of vitamin-B complex in large doses, at first intravenously and then intramuscularly and orally. Admittedly aneurine alone can be successful (de Wardener and Lennox 1947); but deficiency of one vitamin alone is rare, and giving one vitamin in large doses to a patient with multiple deficiencies may precipitate acute deficiency states of the others (e.g., Bichel and Meulengracht 1941). For instance, pellagra may be induced by giving aneurine or riboflavine to a malnourished person.

Prognosis

The fate of 240 reported cases is summarised in the accompanying table. 72% died. Of those receiving parenteral aneurine, however little or late, 31% died; and of those who were not given aneurine 94% died. Of the 68 survivors, 15 were described as being left with a residual Korsakow psychosis; 12 of them had had parenteral aneurine. The chance of saving a patient's life depends on early and intensive treatment, and thus on early diagnosis. If mental symptoms have already progressed to the confusional state before treatment has begun, memory may not be regained and delusions and confabulation may not cease for several months, or indeed ever.

Summary

Fulminating beriberi developed in a woman resident in Great Britain.

The disorder manifested itself as peripheral neuropathy and later (while the patient was in hospital) as acute Wernicke's encephalopathy, Korsakov psychosis, cardiac failure, and œdema. The patient was later found to have advanced gastric atrophy.

The disorder responded partially to vitamin therapy.

We thank Dr. C. Foster Cooper for performing gastroscopy, and Dr. F. E. E. Sargent for the electromyography.

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New Inventions

A NEW AIRWAY-GAG

FOR many years those who have administered electroconvulsion therapy with relaxants have utilised various forms of gags and airways, very often having to improvise because of the lack of reliability, in some cases, of the existing pieces of equipment. In view of the various difficulties encountered, and the injuries caused to the teeth, tongue, lips, and throat of the patient, it is felt that this new combined airway-gag may fill a real need.

The new airway-gag (see figures) is wedge-shaped, made exclusively of surgical rubber of average consistence, and comprises a thumb-grip; a body through which pass four channels; a flange extending round the thumb-grip and the body; a tongue depressor and retractor. Of the four channels, through which oxygen or other gases may be administered, two are larger than the others and can be used for passing a stomach-tube (up to and including size 14) in unconscious states without dislodging the airway-gag—e.g., in insulin-coma therapy, barbiturate poisoning, and recovery states.

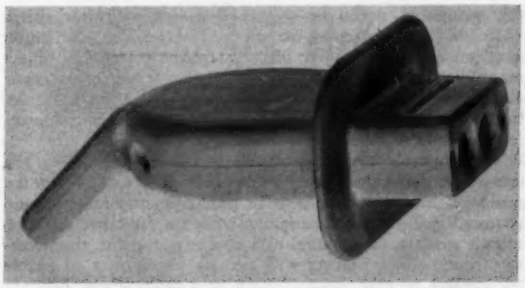
ADVANTAGES

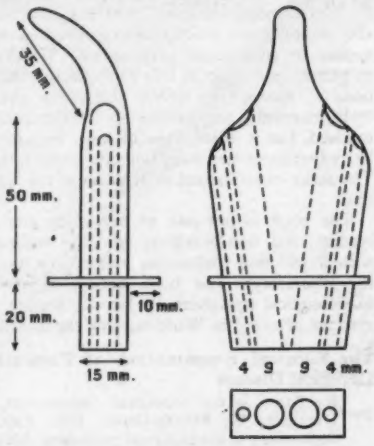
The airway-gag provides retraction of the tongue and reduces stertorous and noisy breathing. It also accelerates pulmonary ventilation and oxygenation.

During an electrically induced convulsion in which muscle relaxaans are used the patient can easily and adequately be protected from biting his tongue and/or lips and getting anoxæmia with increasing exhaustion.

The tongue retractor holds the tongue on the floor of the mouth at all times, thus preventing one of the commonest causes of obstruction of the patient's airway—i.e., allowing the tongue to fall back.

The airway-gag cannot " wobble " in the mouth or occlude its air channels, thus stabilising the patient's respiration.





The tongue retractor and depressor, because of its length, width and thickness, does not touch the pharyngeal wall, and thus trauma to the throat is prevented, and complaints of sore throats (sometimes experienced with airways) are eliminated. The oxygen channels in the airway-gag are relatively short and can thus be easily examined for foreign bodies or unhygienic conditions.

The airway-gag is easily cleaned and sterilised ; it can be used for patients with or without teeth; and it can be used independently, with any apparatus used in electroconvulsive therapy, and with the larger face-masks.

METHOD OF USE WITH RELAXANTS

By gripping the airway-gag with the thumb and index finger of the right hand and holding the tongue retractor pointing downwards there is little difficulty in inserting the airway-gag in the mouth. The tongue retractor can be used to pull the tongue into position on the floor of the mouth, where it will remain during the treatment. The airway-gag is inserted in such a way that the flange is closely apposed to the lips. Sometimes, when the patient has very large jaws and a large mouth, it may be necessary for the flange to be closely apposed to the teeth.

When the airway-gag is in position, the patient's lips are everted on the flange by sweeping one's fingers on the inner surface of the lips and drawing them outwards; this manœuvre prevents undue pressure on the lips and consequent soreness. By applying a little glycerin on a piece of gauze to the lips, cracking of the mucosa (dried by atropine premedication) is eliminated or alleviated, and the lips are easier to evert—this also helps the airway-gag to slide into position more readily.

The airway-gag has been used with both male and female adult patients having all shapes and sizes of jaws and mouths, with edentulous patients, and with those with deficient sets of teeth; but, because of the relatively even distribution of pressure all over the airway and the consistence of the rubber, little impairment of the surrounding structures has been experienced in the past year, during which the airway-gag has been in constant use.

I wish to thank Sir Geoffrey Nightingale, physician-superintendent of Warley Hospital, Brentwood, for help and advice. The airway-gag is made by Messrs. J. G. Franklin & Sons Ltd., 51, Manchester Street, Portman Square, London, W.1.

Warley Hospital,
Brentwood, Essex.

DESMOND C. J. O'CONNOR
L.R.C.P.I.

A PORTABLE URINAL

THE purpose of the apparatus is to allow patients with urinary incontinence or nocturnal enuresis the comfort of a portable urinal that may be worn by day and by night. It is suitable for ambulant or recumbent male or female patients.

It consists of a thin waterproof bag worn under the perineum and between the thighs. The bag is divided into two chambers;

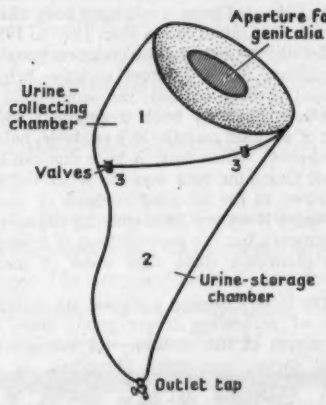


Fig. 1.

the first collects the urine (1, see figure). The second is larger and receives all the urine from the first chamber (2). For female patients the top of the bag is made concave to fit the vulva; for male patients the hole in the top is large enough for the genitalia to be inserted into the first compartment.

To prevent the urine from spilling backwards and overflowing, non-return valves (3) are situated between the chambers. The valves are placed anteriorly and posteriorly in the wall separating these chambers. This allows the patient to adopt any posture without inconvenience or risk of leakage.

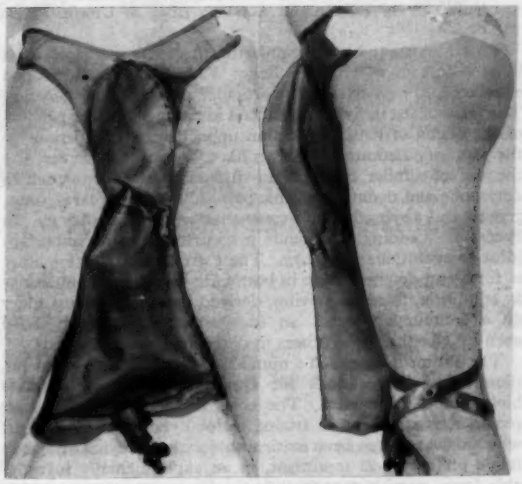


Fig. 2.

After use, the appliance is emptied by a simple outlet tap at the lower end. The whole apparatus is held in position by a halter of webbing around the waist (fig. 2).

Messrs. John Bell and Croyden (Surgical Appliance Department, 50, Wigmore-street, W.1) have manufactured this appliance in three sizes to my design, and it is obtainable from them. It may be prescribed on National Health Service E.C.10 forms.

L. FRIDJOHN,
M.A., M.D. Dubl., M.R.C.P.I.

London, N.8.

Reviews of Books

Chronic Illness in the United States

Commission on Chronic Diseases. Massachusetts: Harvard University Press. London: Oxford University Press. 1957. Pp. 338. 48s.

THIS book is the first of four volumes to be published by the Commission on Chronic Illness, a voluntary body which studied chronic illness in the United States from 1949 to 1956. At the start, the reader may be awed by the countless people involved in this compilation: thirty different societies helped, thirty various technical advisers advised; the commission itself had forty-six members. Yet the book is excellent and presents a vast amount of assorted material in a readable, balanced, and well-set-out manner. When there is little that can be done to prevent chronic illness the book says so. When the cause of an illness is unknown or the accepted methods of treatment are valueless, no space is wasted on discussing improved theories or useless treatments, but the possible lines of fruitful research which might illuminate these dark areas of medicine are indicated.

Yet when the factors causing a disease are understood and the prospects of preventing it are good, there is a clear authoritative survey of the position—for example, in tuberculosis, dental caries, retrolental fibroplasia, or rheumatic heart-disease. Where there are futile preventive measures already in existence their futility is uncompromisingly exposed—e.g., eighteen States forbid epileptics to marry and a federal statute forbids an epileptic to enter the country even for medical advice; and two States forbid a doctor to give advice on contraception.

The work of reducing an almost boundless quantity of mental fodder to assimilable and appetising portions must have demanded exceptional editorial skill, especially since style and humour have remained intact. The book is a valuable contribution to the growing subject of preventive medicine.

The Strategy of the Genes

C. H. WADDINGTON, SC.D., F.R.S., professor of animal genetics, University of Edinburgh. London: Allen & Unwin. 1957. Pp. 262. 28s.

THIS important book extends the theories of organic form in its widest sense, which Professor Waddington has developed elsewhere, to new fields—in particular to population genetics. The form of the individual, reached in ontogeny, is the product of the action of natural selection upon natural populations in the past: populations themselves have "forms", however, and the use of similar concepts in discussing the factors which determine and maintain organic pattern in the two cases, ontogenetic and phylogenetic, is more than an obvious analogy. In Professor Waddington's hands it contributes some important ideas to evolutionary biology. These are based on the picture of form and determination in both individuals and populations as equilibria, fixed or moving, derived from probability states on a contour-landscape, an idea which has already been used by Needham and others in describing embryogenesis.

The author has devised a number of original and, in general, illuminating applications for this concept in evolutionary biology and epigenetics. The chief merit of the book is its remarkable strictness in stating major hypotheses of the sort which have so often been made a subject for edifying or speculative philosophical treatment, in an experimentally investigable form, precise enough to be verified, at least in part, but wide enough in their implications to fill the gaps through which various kinds of vitalism intrude into biological thinking. This is a major feat, and argument at this level calls for a very high order of exposition. The book does not have the flair for making difficult ideas, of which it contains a number, immediately plain, but its quality makes the author fully entitled to expect some work from his readers. Professor Waddington stakes a good deal of his success upon the fitness of the terminology he has devised to clarify his intentions. Some new terms were essential: Waddington's are not uniformly successful, though it would be a thankless task to better them. "Creode", in particular, so spelled, suggests by derivation not "an appointed course of development" but "an object resembling meat", and "homeorrhesis" for homeostasis about a moving point is doubtfully necessary; but these are captious criticisms, and the terminology at least does not interfere with the argument.

Waddington's most important discussion deals with the central paradox of orthodox evolutionary genetics—that on the one hand mutation is held to be predominantly random, and acquired characters not heritable, while on the other selection rapidly produces adaptation to a new environment, the necessary mutations appearing with remarkable aptness to enable the change to take place. There is a definite gap between phenotypic adaptation, which is not inherited, and the heritable adaptations, exactly similar in their expression, which appear in subsequent generations. Waddington's argument in partial resolution of this opposition—one of the "bifurcations of nature" to which Whitehead objected, and which looks inherently improbable—is too detailed to be fairly summarised, but it arises from his own research, and will stimulate experiment for many years to come in many laboratories. The strict experimental orientation of his argument is impressive.

The book is not one to be lightly attempted by general readers, but non-biologists who are willing to take trouble with it will find philosophy restored to its proper context in the laboratory. The book concludes with a more strictly mathematical treatment, by Dr. H. Kacser, of the cybernetic systems involved in Waddington's arguments.

The Clinical Examination of Patients with Organic Cerebral Disease

R. KLEIN M.D., consultant psychiatrist, Crichton Royal, Dumfries; W. MAYER-GROSS, M.D., F.R.C.P., senior fellow, department of experimental psychiatry, University of Birmingham. London: Cassell. 1957. Pp. 96. 15s.

THIS book is less ambitious in its scope than its title suggests, for the authors are concerned with disturbances of the more highly organised forms of behaviour rather than with the more obvious physical defects, such as hemiparesis and visual-field defect, which are so commonly seen in organic cerebral disease. They do, however, give a concise description of the tests by which aphasia, agraphia, alexia, amusia, agnosia, dyspraxia, acalculia, autotopagnosia, and similar disorders can be detected and investigated. They discuss these phenomena sufficiently to explain the tests.

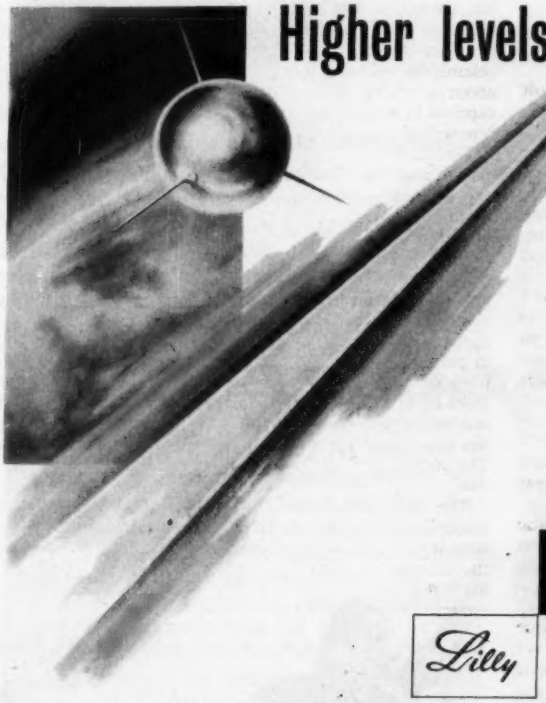
Many doctors who find these disorders hard to understand, and harder to identify in the individual patient, will be glad to have this information, otherwise available only in scattered articles, brought together in one small book. The presentation is as simple as the complexity of the subject permits.

Manual of Stomatology for Dental and Medical Practitioners

J. P. WALSH, M.B., D.D.SC., F.D.S. R.C.S., professor of dentistry, dean and director, University of Otago Dental School. New Zealand: N. M. Peryer. London: Lloyd-Luke. 1957. Pp. 130. 30s.

THIS small book covers all that a medical student needs to know on the purely dental aspects of the mouth. There is also a general survey of the oral manifestations of systemic disease which will serve as a reminder to doctors but is not sufficiently descriptive to be much help to the dental surgeon. The line drawings are good and the photographs excellent—and their quality may be reflected in the price of the book.

Drug Resistance in Micro-organisms (Ciba Foundation Symposium. London: J. & A. Churchill. 1957. Pp. 352. 50s.).—Concerned at the lack of basic knowledge and the empiricism of the clinical approach to chemotherapy, Sir Charles Harington suggested a symposium to the director of the Ciba Foundation. He took the chair at a conference held last March; and the papers are here edited by Dr. G. E. W. Wolstenholme and Miss C. M. O'Connor.



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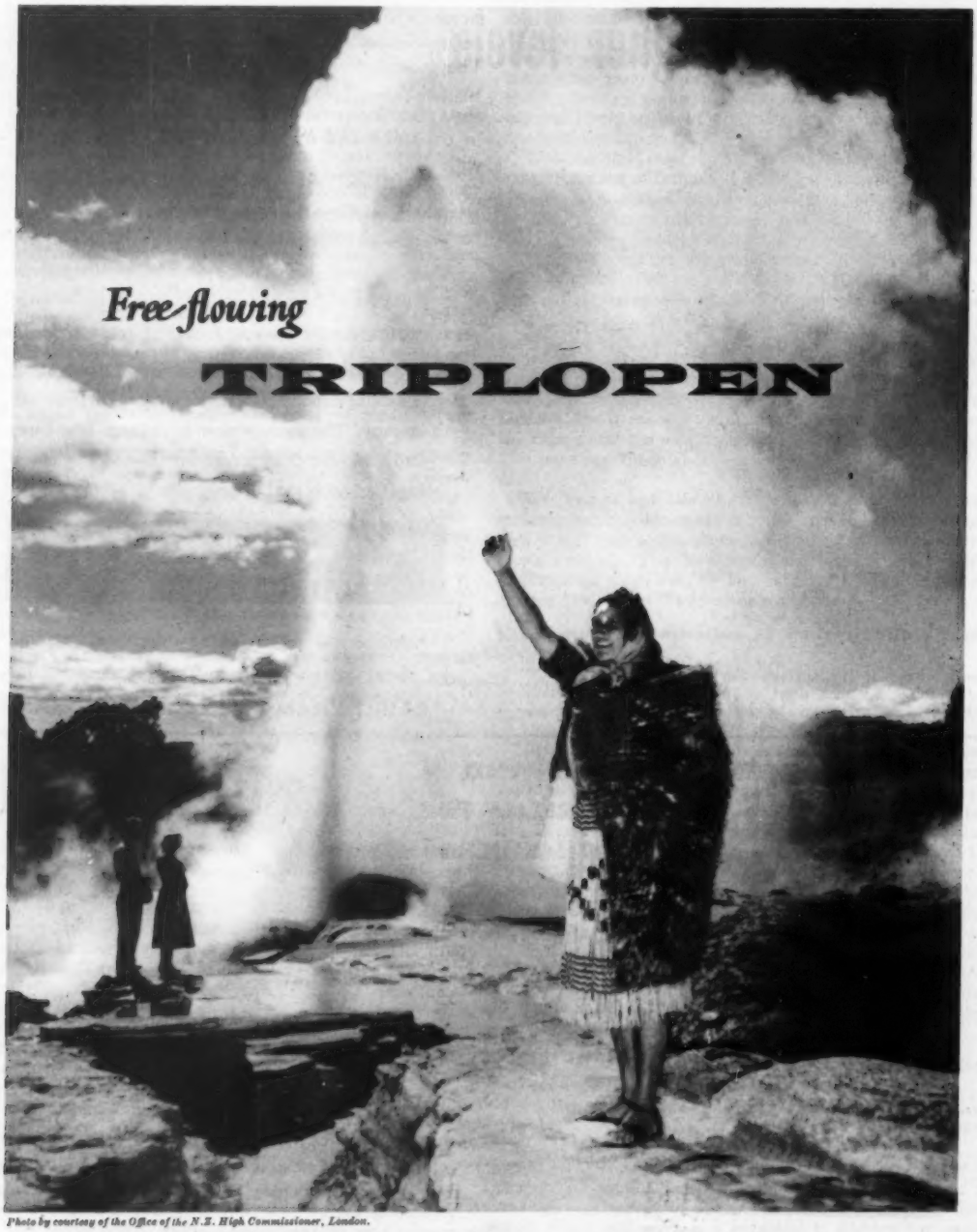

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THE LANCET
LONDON 15 FEBRUARY 1958

Leucocyte Agglutinins and Blood-transfusions

AGGLUTININS that affect red blood-cells are familiar to all; agglutinins that involve blood-platelets have been known and studied for some time; but agglutinins that cause aggregation and possibly destruction of leucocytes have been studied for only a few years, and the idea that leucocyte agglutinins may be responsible for transfusion reactions has appeared quite recently. Leucocyte agglutinins were first identified by MOESCHLIN and WAGNER,[1] in 1952, in the blood of a patient who had agranulocytosis caused by amidopyrine; later in the same year a similar report was published by DAUSSET and NENNA.[2] DAUSSET and his colleagues at the Centre National de Transfusion Sanguine in Paris have carried out considerable research into the detection, properties, and incidence of leucoagglutinins.[3]

All who have worked on leucoagglutinins emphasise the importance of adopting a technique that gives reproducible results and can be properly controlled. Leucocytes for use in the tests are obtained by sedimentation from defibrinated blood after the addition of polyvinyl pyrrolidone or dextran; blood compatible with the serum to be tested must be used to avoid false results due to agglutination of red cells. The test serum is first heated for 10–30 minutes at 56°C; the leucocyte suspension is added and the mixture put in an incubator at 37°C for an hour. It has been found that for easy reading a leucocyte suspension of 5000 to 10,000 per c.mm. should be used. The mixture is examined with a low-power microscope, and the result reported as negative or in various grades of positive. DAUSSET et al.[3] discuss the pros and cons of various alternative techniques and point out that the use of siliconed glassware will give false negative results.

The leucocyte agglutinins so far found are all isoagglutinins—i.e., they do not react with the leucocytes of the patient himself but only with other persons' normal leucocytes; autoleucoagglutinins have not been convincingly demonstrated, and DAUSSET [4] failed to find evidence of autoactivity in the sera of 26 patients who had leucoagglutinins present. Examination of the properties of these leucocyte agglutinins shows that they are relatively thermostable, they can be preserved by freezing, and they are probably, like other antibodies, gamma-globulins. They are most active at 37°C, and their activity can be demonstrated in saline as well as serum media over a wide range of pH from 6.5 to 9.2. They will agglutinate normal and pathological granulocytes and lymphocytes, and can be shown to be absorbed from serum by leucocyte suspensions; their action on primitive leucocytes is uncertain. DAUSSET et al. have shown that serum contains a thermolabile factor which inhibits leucoagglutinins, and this is destroyed by heating to 56°C for up to 30 minutes. The immune nature of the leucoagglutinins, already suggested by their gamma-globulin character and their absorption by normal leucocytes, was further confirmed by their passive transfer. DAUSSET et al. injected serum with leucoagglutinin activity into two recipients; in each case there was a rapid and profound fall of the recipient's white-cell count; whereas injection of normal serum had no effect. Some workers have concluded that human leucocytes possess A and B antigens like those found in erythrocytes; RIIS,[5] for instance, reported that human leucocytes clumped together in anti-A or anti-B sera in accordance with the ABO groups of the leucocyte donors. But doubt has been thrown on the validity of this sort of result by the more recent studies of BAKEMEIER and SWISHER,[6] who have shown that erythrocyte "ghosts" can be demonstrated in the leucocyte clumps and may well be responsible for these observations.

In addition to the very few cases of drug-induced agranulocytosis, leucoagglutinins appear to be present in the serum of a miscellaneous group of patients. DAUSSET et al. examined more than 2000 sera; 500 were of patients with various diseases, of whom 102 had leucopenia; of these 102, leucoagglutinins were detected in only 19. These 19 patients comprised 1 case of amidopyrine agranulocytosis, 3 of paroxysmal nocturnal hæmoglobinuria, 2 of acute leukæmia, 1 of Hodgkin's disease and 2 of lymphosarcoma, 1 of Felty's syndrome, 1 of anæmia secondary to congenital angiomatosis, and 8 of chronic refractory anæmia and leucopenia. Other results have suggested that leucoagglutinins are not limited to patients with leucopenia; thus PAYNE [7] examined the sera of 350 patients with various hæmatological diseases and found leucoagglutinins in 38; 26 of these patients had neither neutropenia nor leucopenia. DAUSSET [4] pointed out, however, that nearly all patients with leucoagglutinins in the serum had received multiple blood-transfusions; and of 60 patients with leucoagglutinins, 90% had been transfused several times. Among the 19 patients of DAUSSET et al., all except the patient with amidopyrine agranulocytosis had received transfusions. PAYNE's series of patients with blood diseases included 49 who had had more than ten transfusions; 19 had leucoagglutinins present, 30 had not; she points out that the fact that blood-transfusion is the common factor in so many cases fits in with the finding that leucoagglutinins are isoantibodies and so do not act on the patient's own leucocytes. "From the standpoint of the recipient," says PAYNE, "the presence of an isoleukoagglutinin in his own serum offers an additional factor to be considered in transfusion reactions."

The hypothesis that unexplained transfusion reactions may be due to the presence of agglutinins affecting leucocytes has been explored by BRITTINGHAM and CHAPLIN,[8] who at the same time looked for platelet

1. Moeschlin, S., Wagner, K. *Acta hæmat., Basle*, 1952, **8**, 29.
2. Dausset, J., Nenna, A. *C.R. Soc. Biol., Paris*, 1952, **146**, 1539.
3. Dausset, J., Nenna, A., Brecy, H. *Blood*, 1954, **9**, 696.
4. Dausset, J. *Vox Sanguinis*, 1954, **4**, 190.
5. Riis, P. *Acta hæmat., Basle*, 1955, **14**, 302.
6. Bakemeier, R. F., Swisher, S. N. *Blood*, 1957, **12**, 913.
7. Payne, R. *Arch. intern. Med.* 1957, **99**, 587.
8. Brittingham, T. E., Chaplin, H. C. *J. Amer. med. Ass.* 1957, **165**, 819.

agglutinins. Transfusion reactions that cannot be attributed to unexpected red-cell agglutinins are particularly liable to be troublesome in patients receiving multiple transfusions—say for the treatment of aplastic anæmia. BRITTINGHAM and CHAPLIN selected 5 patients, known to be prone to febrile transfusion reactions, who had received 20–85 transfusions; for a control series they had 5 other patients who had received 2–7 transfusions and had had no recorded reactions. The blood to be given to these two groups was separated by differential centrifuging into two fractions: a leucocyte-rich fraction which contained nearly all the leucocytes and nearly all the platelets as well, and a leucocyte-free fraction which was also almost free of platelets; the two fractions were transfused on separate occasions. The leucocyte-rich fraction caused febrile transfusion reactions in all 5 test patients, and leucoagglutinins against the donor cells were found in the sera of all of them, varying in titre from 1 in 4 to 1 in 512. The leucocyte-free fraction caused no reactions in the test patients. Neither the leucocyte-rich nor the leucocyte-free fractions caused any reaction in the 5 control patients. Platelet agglutinins did not seem to be important; they appeared in any strength in the serum of only 1 test patient.

These findings confirm that leucoagglutinins may well be the cause of hitherto unexplained transfusion reactions, and it is clear that laboratories supervising the preparation of blood suitable for patients known to be liable to these reactions should include examination of the recipient's serum for leucoagglutinins among the tests to be carried out. Anyone proposing to undertake these tests could study with advantage an account by WALFORD et al.,[9] who describe suitable techniques in detail. They consider that the test is reliable provided the following points are adhered to: a strongly positive control (e.g., a high-titre immune rabbit serum) and at least two negative serum controls should be included in each set of tests; a positive test should show definite clumps of agglutinated leucocytes *and* very few leucocytes between the clumps; and the positive result should be consistently reproducible.

If reactions develop in a patient receiving multiple transfusions, and a leucoagglutinin is found in his serum, then the problem of how to give blood free, or almost free, from leucocytes has to be considered. A differential centrifuge method such as that of BRITTINGHAM and CHAPLIN can be used; but this involves a refrigerated centrifuge, and they had the advantage of using blood collected in plastic bags. CHAPLIN is testing an alternative method which does not involve centrifugation; in this method the red blood-cells are sedimented in dextran, and effective removal of 95% of the buffy coat with retention of 98% of the donor red cells for transfusion is claimed. We hope that this method will pass its clinical trials, because these patients, though relatively few, present an increasing problem now that long-term programmes of repeated blood-transfusion can be undertaken by so many hospitals.

9. Walford, R. L., Peterson, E. T., Doyle, P. *Blood*, 1957, **12**, 953.

Mitral Stenosis and Mitral Incompetence

THE distinction between mitral-valve obstruction and regurgitation has assumed great practical importance. Rheumatic endocarditis involving the mitral valve may produce pure stenosis, free regurgitation, or obstruction combined with incompetence. There is a wide spectrum between the extremes of pure severe stenosis and gross incompetence unaccompanied by narrowing of the valve orifice. Usually pure stenosis gives rise to an easily recognised clinical picture, and can be readily distinguished from pure incompetence.[1] Difficulty in exact diagnosis arises when stenosis and incompetence coexist. Mitral valvotomy, which gives striking relief in pure stenosis, may be valueless or even harmful when incompetence is severe. Differentiation is therefore important; in WOOD'S [2] series of 300 unselected cases of mitral-valve disease mitral incompetence was the dominant hæmodynamic lesion in 34%; in half of these stenosis was also present but was dominated by incompetence.

Much study has been directed to the accurate assessment of stenosis and incompetence, and MCDONALD and his colleagues [3] have lately reported an intensive clinical and hæmodynamic study of 44 patients with severe symptoms due to mitral disease who required surgical relief. The mitral regurgitant flow was calculated from preoperative cardiac-catheterisation data, and from the estimated valve size at operation.[4] The valve size and regurgitant flow were compared with the clinical, radiographic, and electrocardiographic signs.

The clinical history did not differentiate between dominant stenosis and incompetence. Fatigue, in addition to dyspnœa, was found in all types of case and was thought to be due to a low cardiac output. Hæmoptysis was rather less common in dominant incompetence than in dominant stenosis, and a history of systemic embolism was not obtained from patients with the largest valves. On examination, the signs of severe incompetence tallied well with the usually accepted criteria: a localised thrusting cardiac impulse denoting left ventricular hypertrophy, a normal or soft first heart-sound at the apex, a third heart-sound, and a pan-systolic apical murmur conducted to the axilla. The arterial pulse was of smaller volume in patients with pure severe stenosis than in those with dominant incompetence. There were, however, exceptions. A third heart-sound was detected in 4 patients with severe stenosis, instead of the usual opening snap. Damping of the first sound and opening snap is sometimes referable to calcification of the valve.[5] MCDONALD et al. emphasise the importance of the opening snap in the diagnosis of stenosis [6]; a loud snap suggests a pliable valve amenable to surgery. They do not comment on the timing of the snap, which is now generally held to be of value in determining the degree of stenosis: the earlier the snap after the second heart-sound, the tighter

1. Brigden, W., Leatham, A. *Brit. Heart J.* 1953, **15**, 55.
2. Wood, P. *Brit. med. J.* 1954, **i**, 1051, 1113.
3. McDonald, L., Dealy, J. B., Rabinowitz, M., Dexter, L. *Medicine, Baltimore*, 1957, **36**, 237.
4. Gorlin, R., Dexter, L. *Amer. Heart J.* 1952, **43**, 188.
5. Wynn, A. *Brit. Heart J.* 1953, **15**, 214.
6. Mounsey, J. P. D. *ibid.* p. 135.

the stenosis.[7] The typical mitral diastolic murmur was present in all patients save one, but its intensity was not related to valve size. The length of the murmur was thought to be proportional to the severity of the stenosis. Apical systolic murmurs were louder in patients with significant incompetence than in those without; but soft systolic murmurs were heard in patients with pure stenosis, if atrial fibrillation was present. When gross incompetence was present a loud systolic murmur was heard, and absence of such a murmur virtually excluded incompetence. In intermediate cases the intensity of the systolic murmur did not indicate the degree of incompetence. It is important to distinguish the pansystolic murmur of mitral incompetence from that of tricuspid incompetence, and from the ejection murmur of aortic stenosis.

Radiographic studies confirmed the clinical findings of enlargement of the right ventricle in pure stenosis, and of the left in pure incompetence. Enlargement of the right ventricle was greatest in patients with the smallest valves. Left ventricular enlargement usually indicated significant incompetence but was present in 4 cases with pure stenosis, in the absence of any other cause. The right ventricle was enlarged in mitral incompetence when the pulmonary resistance was raised, and McDONALD et al. point out that such enlargement does not exclude the presence of severe incompetence. The size of the left atrium was not helpful in assessing valve size; severe incompetence was usually accompanied by a large left atrium, but this was occasionally seen with pure stenosis, as others have found.[8 9] Systolic expansion of the left atrium was of no value in distinguishing incompetence from stenosis. Calcification of the mitral valve was common but was not specially associated with incompetence—a finding which differs from that of WYNN.[5] Little differential diagnostic help was apparently gained from radiographic signs of pulmonary venous and arterial hypertension[10 11]; perhaps this is so because the lung changes correlate best with increases in pulmonary vascular resistance, which can be present in both incompetence and stenosis.

The electrocardiogram showed evidence of right ventricular hypertrophy in pure severe stenosis when the pulmonary vascular resistance was appreciably raised, but of left ventricular hypertrophy in severe incompetence. In intermediate cases there was evidence of biventricular hypertrophy or normal ventricular balance. Broad and notched " mitral " P waves due to left atrial enlargement did not differentiate between incompetence and stenosis, but atrial fibrillation was universal in the cases of frank incompetence, whereas many with pure stenosis had sinus rhythm. Hæmodynamic studies showed that when mitral disease was severe the dominant lesion (stenosis or incompetence) was closely related to forward mitral-valve area. Significant incompetence was exceptional with the smallest valves, while dominant incompetence was the rule with the larger valves. Between the extremes was a wide spectrum in which dominant stenosis shaded gradually into dominant incompetence. Pulmonary vascular resistance was highest in patients with pure stenosis, but considerable increases in resistance were also found in incompetence. Like other workers,[12] McDONALD et al. obtained little diagnostic help from the form of the pulmonary capillary venous pulse, a large v wave often being found in both stenosis and incompetence. They hold that more information is needed about the estimation of the rate of descent of the y wave, expressed as the " Ry/v ratio " of OWEN and WOOD.[13] But a slow " y " descent is helpful in suggesting mitral obstruction.

This valuable contribution lends weight to the accepted criteria for the diagnosis of mitral incompetence, and suggests that combined clinical, radiographic, and electrocardiographic examination usually provides the best estimate of the relative contributions of stenosis and incompetence. But difficulty exists in many cases, and the refinements in diagnostic method still needed may be provided by the dye-dilution techniques of KORNER and SHILLINGFORD.[14] Other techniques, involving puncture of the left atrium[15–17] and consecutive measurements of left atrial and ventricular pressures, may yield useful information; but simultaneous measurement of flow is necessary for diagnostic certainty.

Epilepsy and Hysteria

FASHIONS in disease are imposed not only by medical opinion but also by the *Zeitgeist*. Few doctors now see *la grande crise d'hysterie*—the major hysterical fit which used to be an important and sometimes difficult differential diagnosis from epilepsy. CHARCOT,[18] in the dawn of modern clinical neurology, made the distinction with his usual clinical shrewdness, and the main differences that he noted continue to guide us. There were cases, however, in which he found it hard on semeiological (and, one suspects, on ætiological) grounds to separate the two. These he referred to as " hystero-epilepsy ". The term and the concept were not generally accepted by a later generation of French neurologists. BABINSKI,[19] for instance, insisted that all cases could be put into one or other category. BUMKE[20] in Germany was equally emphatic. ALDREN TURNER[21] in this country was less dogmatic: but in general hystero-epilepsy was regarded with suspicion. The ætiological segregation of the two conditions—and this was the real point at issue—was considered to be complete. The problem was shelved rather than solved, and KRAPF[22] has lately reviewed it.

Diagnosis has always been difficult in the cases with

7. Wells, B. *ibid*, 1954, **16**, 261.
8. Venner, A. *Brit. med. J.* 1954, i, 1359.
9. Goodwin, J. F., Hunter, J.D., Cleland, W. P., Davies, L. G., Steiner, R. E. *ibid.* 1955, ii, 573.
10. Davies, L. G., Goodwin, J. F., Steiner, R. E., Van Leuven, B. D. *Brit. Heart J.* 1953, **15**, 393.
11. Short, D. S. *ibid.* 1955, **17**, 33.
12. Wynn, A., Matthews, M. B., McMillan, K. R., Daley, R. *Lancet*, 1952, ii, 216.
13. Owen, S. G., Wood, P. *Brit. Heart J.* 1955, **17**, 41.
14. Korner, P. I., Shillingford, J. P. *Clin. Sci.* 1955, **14**, 553.
15. Radner, S. *Acta med. scand.* 1955, **152**, 1.
16. Morrow, A. G., Braunwald, E., Haller, J. A., Sharp, E. H. *Circulation*, 1957, **16**, 399.
17. Björk, V. O. *Acta chir. scand.* 1954, **107**, 466.
18. Charcot, J. M. Lectures on Diseases of the Nervous System. London, 1877.
19. Babinski, J. Ma conception de l'hysterie. Chartres, 1906.
20. Bumke, O. Handbuch der inneren Medizin. Berlin, 1926.
21. Turner, W. A. Epilepsy. London, 1907.
22. Krapf, E. E. *Bull. Wld Hlth Org.* 1957, **16**, 749.

features of both epilepsy and hysteria; and it was usual to suggest that hysteria happened to coincide with epilepsy, just as it might with any other organic condition. In some cases the concept of "affective epilepsy"—a form of reflex epilepsy in which the afferent stimulus was an emotional one—was a help, but many could not be forced into this mould. With the advent of the electroencephalogram (E.E.G.) the differentiation should have become easier; for if epilepsy is a specific cerebral dysrhythmia this can surely be recognised on the E.E.G., and if the dysrhythmia is not present the attacks cannot be epileptic. Unfortunately, with growing knowledge of the E.E.G., this argument is not as convincing as it was. E.E.G. records are still useful diagnostically, but it has become clear that some abnormalities are not a specific epileptic dysrhythmia but are somewhat similar to such dysrhythmia; and commonly these are found in just those patients whose abnormal behaviour raises the possibility of a psychiatric diagnosis. Thus aggressive psychopaths, and indeed inadequate psychopaths too, in whom hysterical features are readily found, have abnormal E.E.G.s which represent in part a defect of "maturation" of the electrical record. In aggregate these can probably be distinguished from a group of epileptic records, but distinction in individual cases may be very hard.

Growing recognition and exploration of the temporal-lobe group of epilepsies further obscures the borderline. (CHARCOT's own description of hystero-epilepsy reads very like an example of temporal-lobe epilepsy.) Here undoubted epilepsy occurs in a setting of behaviour disorder and emotional abnormality, and individual fits sometimes appear to have a mental cause. Indeed, for epilepsy in general BARKER [23] and others have made the wider claim that with abreactive and suggestion techniques an appropriate psychological stimulus will reproduce specific epileptic activity, both electroencephalographic and clinical. Conversely formal psychotherapy, particularly where specific psychogenic features can be uncovered, may very occasionally have a dramatic effect on epilepsy; and the psychotherapy of environmental adjustment may be more often effective though less dramatic.

It seems that we must reconsider the concept of hystero-epilepsy, not in the form that CHARCOT put it forward, but as a more fundamental problem in the physical and mental genesis of epilepsy. The clinical problem may be small; but the idea behind it is important. In these days of psychosomatic medicine it is as well to try and see the reality behind the phrase.

23. Barker, W. *Res. Publ. Ass. nerv. ment. Dis.* 1950, **29**, 90.

Annotations

TRUANTS IN INDUSTRY

Shepherd and Walker [1] have studied the relation of absence from work and overtime working, on the one hand, to wage level and the number of dependants on the other. Their investigation was made in 1952 in a large iron and steel works where wage differences depend on promotion grades and do not sharply reflect differences in skill or responsibility, and bonuses bear little relation to individual productivity. The difference in gross annual wages between the highest and lowest paid groups was £300. The data were taken from absence records; nearly equal numbers of men were selected in each of six wage-groups, matched for average age, income-tax code-number (as an index of the number of dependants), heaviness of work, and temperature of working conditions. The number of absences and total duration of absence (as number of shifts lost) were calculated per 100 men in each group, and divided into absence due to sickness, due to injury, with permission, and without permission.

Certain trends were obvious. The absence-rate was high in the lowest-paid group, mainly through more absences without permission and more long absences with permission. In other groups the number of absences and of shifts lost increased with increasing wages. Absence without permission increased with increasing wages, but this did not hold for the highest and lowest wage-groups. At higher wage levels the high total number of absences was caused by absences without permission, but the large number of shifts lost was caused mainly by more recorded sickness. There was no evident a-priori reason to expect a greater incidence of sickness in the higher-paid group (indeed, in an outbreak of influenza the previous year the incidence had been much higher in the lower-paid workers). Shepherd and Walker believe that the difference was caused by a greater tendency to go absent (for illness or other reason) and a tendency to stay away longer for a given illness in the higher-wage group, and by differences in reporting illness. At lower wage levels many absences of medium length were probably due to sickness, though not reported as such. Thus there were many more absences (recorded as "without permission", not as "due to sickness") of four to nine shifts' duration than of two or three shifts' duration; this would accord with their being caused by sickness, because of the National Insurance sickness-benefit regulations.

Absence-rates also varied according to family responsibility: they were high for single men, lowest for those with two dependants, and higher again for those with more; this was true for both the higher-paid and the lower-paid workers. The amount of overtime worked increased with number of dependants in the case of the lower-paid workers, but there was no such relationship among the higher-paid workers—perhaps partly because of income-tax differentials. The lowest-paid group had the highest overtime figures as well as a high absence-rate.

Shepherd and Walker differentiate between an individual "absence threshold", determined by long-term factors, both personal and general, and the immediate factors which raise the question of whether or not to go absent and may be powerful enough to exceed the threshold. One step towards "coping with absence", they say, lies in discovering the associations between absence and such factors as number of dependants, time of day (e.g., single-shift absences without permission have been shown to be commonest in the morning shift [2]), or day of the week. Their investigation indicates that wage-level is an important factor.

1. Shepherd, R. D., Walker, J. *Brit. J. industr. Med.* 1958, **15**, 52.

2. Shepherd, R. D., Walker, J. *occup. Psychol.* 1956, **30**, 105.

Discussion of absence from industry nearly always starts from the point of view of employers, whether private or public, or of society as a whole ; and strong pressure may be put on individual workers to stay at their jobs unless circumstances are exceptional. Dr. D. H. Stott [3] finds that this pressure is likely to increase:

> " We have to recognise that the static, self-indulgent pattern of living is out of place in the modern world. If one of a gang of roadworkers stayed at home to tend his pigeons the loss would be just that of his day's labour. But now excavating is done by mechanical monsters; if the trained man working one takes a day off the whole job is held up."

At present, absence from work is especially common, and especially deprecated, in coalmining—which, as has been lately pointed out,[4] is one of the few remaining industries where a man can earn enough to afford an occasional unpaid day's leisure if the fancy takes him; and which therefore attracts men to whom this freedom appeals. The anxiety felt about absence from work stems largely from society's overwhelming need to increase production in a competitive or warring world. But from the individual's point of view, it will be a poor world if we became rich in the goods produced by industry at the expense of being tied rigidly to our work. That, rather than conquest by " universal robots ", might be the way in which machines could come to dominate us—not only the mechanical devices for production but the mechanical organisation of society.

REFLEX ANURIA

SUPPRESSION of renal function occasionally follows instrumental procedures on the renal tract, or the sudden relief of chronic urinary retention; it may arise in an apparently healthy kidney when the contralateral organ becomes acutely obstructed, as by a calculus; and rarely it follows certain gynæcological and obstetric operations in which the urinary tract has not apparently been primarily involved. To this condition, with such diverse causes, the name " reflex anuria " has been given; and it has generally been assumed to be caused by excessive stimulation of the sympathetic nervous system, which induces either reflex renal ischæmia or overproduction of pituitary antidiuretic hormone. The possibility that some cases may be due to postrenal obstructive causes has tended to become overlooked; and, since the oliguria is often transient, the need to inquire further seldom arises.

Sirota and Narins [5] report three cases in which an obstructive lesion was evident, in the form of gross bullous œdema at the ureteric orifices. In two of these cases both ureters had previously been catheterised in the normal way; in the third case nephrectomy had been carried out shortly after catheterisation of the opposite side. In all three cases severe oliguria and progressive azotæmia and hypertension had followed the ureteric manipulation. A second cystoscopy confirmed the presence of obstruction due to œdema at the orifices, with absence of normal effluxes; and in each case the condition was relieved by the reinsertion of indwelling ureteric catheters. Since there was no apparent technical difficulty at the time of the initial investigation, Sirota and Narins conclude that the œdema may have been induced by an idiosyncratic response to trauma, to the formaldehyde used for catheter sterilisation, or to the contrast medium used for retrograde pyelography.

Such sensitivity can be assumed to be rare; but these cases are a reminder of the need for preliminary inquiry and for careful washing of all the instruments before making this commonplace examination.

3. Stott, D. H. Present Needs in Our Work Among Youth. London, 1958. See *Lancet*, Feb. 8, 1958, p. 305.
4. See *Observer*, Jan. 5, 1958.
5. Sirota, J. H., Narins, L. *New Engl. J. Med.* 1957, **257**, 1111.

SALARIES OF HOSPITAL EMPLOYEES

THE National and Local Government Officers Association (NALGO) [1] have surveyed the salaries and work of more than a quarter of all administrative and clerical workers in the National Health Service to find that 36% earn less than £400 a year, 46% earn £400–£600, 10% earn £600–£800, 5% earn £800–£1200, and 3% over £1200. More than 80% are thus earning less than the weekly £12 1*s.* 6*d.* earned by a male manual worker. The modest rises which these workers have received over the past ten years have not been enough to keep pace with inflation. Thus though a man who was earning £385 in 1948 is now earning £515 the cash value of his earnings would have been only about £325 in 1948. Compared with his colleagues on the same salary in other services he has had a poor deal. His effective salary has fallen by 15% compared with 1% in the Civil Service.

The Guillebaud and the Hall Committees, both valuable outside opinions, have confirmed the inside opinion of hospital administrators that the present rates of pay are threatening efficiency and injuring recruitment, yet NALGO's survey shows that few offices are " seriously below establishment ". This may perhaps mask some of the dangers of the situation. The posts are apparently only being filled after repeated, and expensive, advertisements. Too many of the staff are drawn from elderly retired men and married women. These workers are often skilled and conscientious and their help is valued, but they are not " promotion material " The few young people who join the service do not stay and are often unsuitable. Older men and women who find the work satisfying and who have pension rights are understandably less likely to leave, though even in this group there have been some reluctant defaulters. At present they are overworked and spend too much of their time training the constantly changing junior staff, and checking and supervising their work. NALGO's survey gives as examples of this overbrisk turnover a south-eastern hospital group that has replaced a third of its staff in two years, a London group that has replaced two-thirds in the same period, and a west country group that has replaced the whole of its finance department since January, 1955.

The present economy in salaries seems to be causing not only inefficiency but also extravagance. Advertising over the whole country must, it is estimated, cost about £500,000 a year. Agency typists are often employed as stop-gaps and earn more money and work shorter hours than the permanent staff.

The recommendations of the Hall report,[2] which are at present being considered by a joint sub-committee of the Whitley Council, would do much to right the situation. It is important that the hospital service should be able to attract and retain its fair share of competent young men and women who will be willing and able to take advantage of the opportunities for training and promotion which it should offer. But we live in a century, to look

1. *Publ. Serv.* February, 1958, p. 38.
2. See *Lancet*, 1957, ii, 1104.

no further, in which there are likely to be more and more old people and fewer young people. The health service would be sensible to remember the help that pensioners and married women have given in these difficult times. Even in easier times they could offer valuable support to the recruits whom we all hope the service will get, and for themselves have the healthy satisfaction of doing a worth-while job.

THE SECOND STAGE

IN these days of strict training for natural childbirth it is widely held that the first stage of labour should normally be a time of rest and relaxation in an atmosphere of quiet efficiency. The time for hard physical effort comes later, in the second stage. A first labour is seldom concluded naturally without at least a short period of pushing by the mother to assist the uterine action. But it is perhaps not always remembered that much of the second stage needs no help from the mother, the uterus alone advancing the presenting part down to the perineum. A patient who is urged to push too early in the second stage may achieve little which could not be done as well by the unaided uterus, her exertions leaving her exhausted towards the end of her labour when her efforts are required. Constance Beynon[1] believes that there are other disadvantages both to too early and to too vigorous pushing. She points out that the secondary powers applied while the presenting part is still gripped by the cervix or the upper vagina—broadly the site of insertion of the transverse cervical ligaments—will produce on these important supporting structures a downward thrust which may well be a significant factor in the causation of vault prolapse. Similarly, straining efforts made while part of the anterior vaginal wall is below the head may result in this part of the wall being rolled down beneath the head with potential damage to the underlying structures around the bladder base, perhaps leading to stress incontinence. Mrs. Beynon believes that these tendencies will be slighter in the absence of straining efforts, since the early part of each contraction pulls the vagina taut and prevents it and the structures deep to it being pushed down in front of the presenting part. She likens the process to a sleeve with a loose lining: the slower the arm is passed down the sleeve the less the tendency for the lining to roll out at the wrist, especially if the lining is held firmly at the top.

Theoretical considerations apart, Mrs. Beynon's method of allowing the patients to follow their own inclinations in the second stage of labour, forbidding any mention of pushing by those in attendance, seems to prove its worth in practice. In a clinical trial a much shorter period of pushing and a lower forceps and perineal-laceration rates were found in patients managed in this way than in a second group more actively encouraged to push the child out. Although, because of variable factors, this was not strictly a controlled trial, the method seems to have much to commend it. Thus, the atmosphere of tranquillity which she describes in the second stage contrasts sharply with the scenes of violent muscular effort when the "labouring" woman is persistently urged to take an active part.

For the normal case this policy of non-intervention seems reasonable. There are circumstances, however, in which the vigorous cooperation of the patient can contribute significantly to the safe delivery of her child. Breech delivery, for instance, achieved by the patient's efforts with minimal interference by the attendants is greatly to be preferred to breech extraction under general anæsthesia. Rarely in the multipara the pains will almost disappear in the second stage, leaving the head stationary in the middle or lower part of the pelvis; and here, as with the breech which the patient cannot quite push over the perineum, brief adoption of the squatting position may have dramatic effects.

1. *J. Obstet. Gynæc., Brit. Emp.* 1957, **64**, 815.

ARMY MEDICAL HISTORY ON SHOW

IT seems that in this country few museums, apart from the famous national ones, can be said to prosper[1]; and if many of the rest are ill attended it may be because they are ill tended. But no such accusation can be laid against the R.A.M.C. Historical Museum, at Crookham. Built up in the past five years by Major-General R. E. Barnsley, who remains the curator, this collection sparkles; and its existence should be more widely known.

The collection is mainly for the non-specialist: the muniments section is held elsewhere (at the R.A.M. College, Millbank); and no effort has been made to duplicate the purely technical collections that were already in being. But, without entering into technicalities, this group of apparatus, models, plaques, letters, drawings, photographs, standards, medals, and so on illustrates brilliantly the development of the Army medical services from the time of the Peninsular War, in which the Duke of Wellington had miserably small medical resources at his command, down to and beyond the war of 1939–45, with Field-Marshal Montgomery writing soon after its termination of a Corps "whose contribution to victory has been beyond all calculation".

The medical relics include "Dr. Wilde's electric alarum indicator with insulated explorer and forceps," which puts far back into the 19th century the date when metallic foreign bodies—in this case bullets—were first localised electrically.[2] There is a wealth of paramedical objects—including a letter from the indefatigable Miss Nightingale, who took time off at Scutari to communicate at some length with a young admirer in England. Also on view is a quilt knitted by Queen Victoria for patients at Netley Hospital. (There is an old story, probably apocryphal, that this was applied only to fortify the dying, but, as this became widely known, its single purpose may not have been wholly achieved.) Inevitably, too, the museum shows something of our military history proper. (Who knows the origin of "Thomas Atkins"?) And for the unwarlike it provides welcome evidence of evolution from the days, not so long ago, of the cat-o'-nine-tails, of branding deserters, and of "crime-and-punishment" books whose every page is filled with charges of drunkenness.

The collection reveals doctors, in war and in peace, as incorrigible magpies: the trophies range from a Russian drum won at Sebastopol to a Coptic cross collected by a surgeon in Lord Napier's Abyssinian Campaign of 1868. Perhaps the keenest medical collector of all is General Barnsley himself, who (ignoring the adage that good wine needs no bush) is at present bent on discovering a pre-1914 horse-drawn heavy ambulance-wagon to place outside the museum—perhaps hoping thus to distinguish it, for the benefit of visitors, from the commandant's office nearby. Any reader lighting on a disused horse-drawn heavy ambulance-wagon in his garage is invited to offer it to the museum.

The museum is open to the public on Mondays to Fridays from 10 A.M. till noon and from 5 till 7 P.M., and on Saturdays from 10 A.M. till noon. Visitors are welcome at other times, including Sundays, but are asked to write in advance to the Curator, R.A.M.C. Historical Museum, Queen Elizabeth Barracks, Crookham, Hants.

1. See *Manchester Guardian*, Feb. 5 and 6, 1958.
2. See Suffern, C. *Lancet*, 1957, ii, 1174.

Special Articles

INCIDENCE OF WOUND INFECTION

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FOR some time the surgeons at the Edinburgh Royal Infirmary have been concerned with the frequency with which their operation wounds become infected. As in many other old-established hospitals, the operating-theatres of the Infirmary are under suspicion because of out-of-date sterilising equipment and inefficient ventilation systems. Before major improvements were started, we thought it desirable to know the present incidence of wound infection which would serve as a basis for comparison in the future; and in addition we hoped that this survey would help us in formulating a satisfactory routine method of recording infection for our hospital.

The true figures of wound infection in a busy hospital are more difficult to obtain than appears at first sight. There is the possibility that the incidence will vary at different times of the year, month, or week. This means that records should be kept over an entire year and in greater detail than is customary in the patient's case-record or in a "wound book". The practice of keeping a wound book is good, but to measure the incidence of wound infection from it can be misleading because the entries in the book and the abstraction of the information are usually done in retrospect and may not give a complete account of the infection. Anything less than frank sepsis is apt to be omitted. There are also administrative problems in ensuring that the wounds are followed up over a sufficiently long time and with sufficient care to know whether or not infection has in fact taken place. This may be particularly difficult when surgical cases are transferred to convalescent homes, sometimes a few days after operation, with a consequent break in the continuity of observation and recording. Finally, the criteria of infection and degree of infection have to be established and made uniform throughout the wards where the recording is being done.

Procedure

The investigation was made in four surgical charges: the neurosurgical charge, the orthopædic charge, and two general-surgery charges for three months from October to December, 1956. Every case passing through the operating-theatres of these charges was followed up meticulously, and the wound, whether incisional by operation or accidental, was assessed as regards cleanliness and infection while healing. It was decided to make the assessment of infection entirely clinical, but provision was made whereby particulars of bacteriology and chemotherapy could be correlated later.

Precoded forms were printed and kept in the operating-theatre precincts, and on completion of the operation the surgeon or one of his assistants filled in the main particulars—e.g., name and age of patient, type of operation, and nature of the wound. While the patient remained in hospital the forms were kept with the patient's case-notes.

The method of current recording of the state of the wounds varied a little from ward to ward, but in all wards, whenever an infection was noted by superficial inspection or on removal of stitches or at any dressing, this was recorded at the time and not retrospectively. These observations in the ward were usually made by the ward sister in the course of her dressing rounds, and one useful means of immediate recording was to make a small symbol on the temperature chart at the bedside. Routine checks on the methods of assessment and consistency of recording were made by the surgeons in charge of the investigation.

When a patient was transferred to a convalescent home or other hospital, a second form, identical with the original, was filled up separately and independently by the doctor at the receiving hospital or home. Thus duplicate records were kept for these transferred patients, and in this way it was possible to have a check on all wounds and to ensure proper follow-up.

Where a second operation on the same patient involved a fresh incision, a separate form was completed for each operation. There were 20 second operations, representing 2·8% of the total records.

Multiple wounds at one operation were recorded for 12 cases. To avoid difficulties in the analysis, these were regarded as single wounds, and only one form was completed for each case. This study covers, in all, 708 wounds.

After final discharge of the patient with his wound soundly healed (usually at six weeks), the information was transferred to Powers-Samas punch cards for analysis.

Criteria of Assessment

In this investigation the wound state was assessed under two main headings and, so far as was humanly possible, uniform criteria were adopted by the participating medical and nursing staffs. The first heading concerned the *nature of the wound*, and by this was meant whether the wound at operation was clean, clean but potentially infected, or frankly infected. This decision lay entirely in the judgment of the surgeon. The "*clean*" wounds were "cold" orthopædic and neurosurgical cases, thyroidectomy, herniotomy, &c. In the "*potentially infected*" group were cases of acute non-perforated appendicitis and cases where the gastrointestinal tract had been opened at operation—e.g., at colectomy and at gastrectomy. The "*frankly infected*" were cases of ruptured appendicitis, abscesses, &c.; these cases were dirty at operation and in the event remained so.

The second heading dealt with the *degree of infection* in the subsequent wound, and the degree was assessed as none, trivial, moderate, or severe. The definition of these terms was as follows: *none*, a dry clean wound without redness; *trivial*, redness at the wound edge or stitch holes; *moderate*, definite signs of inflammation, including a little purulent exudate; and *severe*, frank copious pus.

Results

The 708 wounds from the four charges—orthopædic, neurosurgical, and two general-surgery—were associated with a wide variety of common operations. In table I the records are analysed in terms of "the type of wound at operation", the "nature of the wound", and the type of surgical charge.

TABLE I—TYPE AND NATURE OF WOUND AT OPERATION

Type of charge	Type of wound			Nature of wound			Total
		Accidental					
	Incisional	Single	Multiple	Clean	Potentially infected	Frankly infected	
Orthopædic ..	133	—	—	126	5	2	133
Neurosurgical ..	129	—	—	115	14	—	129
General-surgery I	207	13	8	63	152	13	228
General-surgery II	211	3	4	124	74	20	218
Total	680	16	12	428	245	35	708
Percentage of all wounds	96·0	2·3	1·7	60·5	34·6	4·9	100

TABLE II—PERCENTAGE INCIDENCE OF INFECTION IN CLEAN WOUNDS

—	Ortho-pædic	Neuro-surgical	General-surgery I	General-surgery II	Total
Wounds classified as clean and not potentially infected:					
No. of wounds	(126)	(115)	(63)	(124)	(428)
Trivial ..	3·2	4·3	12·7	13·7	7·9
Moderate ..	0·8 } 0·8	3·5 } 5·2	6·3 } 11·1	4·0 } 4·0	3·3 } 4·5
Severe ..	— }	1·7 }	4·8 }	— }	1·2 }
Total ..	4·0	9·5	23·8	17·7	12·4
Wounds classified as clean but potentially infected:					
No. of wounds	(5)	(14)	(152)	(74)	(245)
Trivial ..	20·0	35·7	29·6	33·8	31·0
Moderate ..	— } 20·0	7·1 } 7·1	15·1 } 18·4	18·9 } 23·0	15·5 } 19·2
Severe ..	20·0 }	— }	3·3 }	4·1 }	3·7 }
Total ..	40·0	42·8	48·0	56·8	50·2
All wounds classified as clean at operation:					
No. of wounds	(131)	(129)	(215)	(198)	(673)
Trivial ..	3·8	7·7	24·6	21·2	16·3
Moderate ..	0·8 } 1·6	3·9 } 5·5	12·6 } 16·3	9·6 } 11·1	7·7 } 9·8
Severe ..	0·8 }	1·6 }	3·7 }	1·5 }	2·1 }
Total ..	5·4	13·2	40·9	32·3	26·1

96% of the wounds were incisional. The 28 accidental wounds were confined to the two general-surgery charges. 63% of the wounds were from the two general-surgery charges; wounds from the orthopædic and neurosurgical charges represented 19% and 18% respectively.

60% of the wounds (428) were classified as clean and free from potential infection at operation; 35% (245) were clean at operation but were regarded as potentially infected; and 5% (35 wounds) were frankly infected. In both the orthopædic and neurosurgical charges most of the wounds were clean and were not regarded as potentially infected. Most of the wounds in general-surgery I were classified as potentially infected, whereas in general-surgery II most of the wounds were clean.

The difference in the proportion of clean wounds regarded as potentially infected in the two general-surgery charges suggest that there might have been differences in the criteria of assessment, because largely the same kind of surgical work is done in these charges. However, we believe that the assessments were fair; otherwise one would have expected that the clean wounds in general-surgery II, where they were in the majority, would have carried a higher infection-rate than the clean wounds in general-surgery I, where they were in the minority. Table II shows that this was not so, and in the analysis of the results the figures from the two general-surgery charges can therefore be merged.

The main results of the investigation are summarised in table II. The 35 wounds which were frankly infected at operation (see table I) and which continued to be septic until eventually healed may be excluded, leaving 673 wounds which were clean at operation and thus at risk to subsequent infection.

The incidence of infection is expressed as a percentage for wounds classified by the surgeon as clean and not potentially infected, for wounds classified by the surgeon as clean but potentially infected, and for all clean wounds. The number of wounds in each group is shown in brackets.

26·1% of the 673 clean wounds were found to be infected at some time after the operation. The infection was recorded as trivial in 16·3%; and too much emphasis need not be given to these trivial infections, because redness at the stitch holes and wound margin might well arise from necrosis by suture material rather than from bacterial infection. Principal attention will therefore be given to wounds which were seriously infected, and for the purpose of this investigation the moderate and the severe infections are grouped together under the term " serious ".

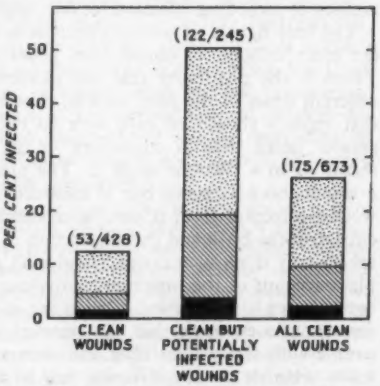
TABLE III—INFECTION-RATES IN DIFFERENT CHARGES

Charge	Wounds	Serious %	Trivial %	Total %
Orthopædic	131	1·6	3·8	5·4
Neurosurgical	129	5·5	7·7	13·2
General-surgery I ..	215	16·3 } 13·8	24·6	40·9
General-surgery II ..	198	11·1 }	21·2	32·3
Total	673	9·8	16·3	26·1

7·7% of the 673 clean wounds (which should not have become infected) showed a moderate degree of infection, and 2·1% became severely infected. The overall incidence of serious wound infection in this series, a combination of these two percentages, is therefore 9·8%.

Table III summarises the infection-rates in the different charges detailed in table II. The incidence of serious infection in the orthopædic charge was relatively low (1·6%) and in the neurosurgical charge rather higher (5·5%), whereas in the general-surgery charges taken together it was as high as 13·8%. In this respect the general-surgery charges overweigh the others, and they are responsible for the high average infection-rate.

In the potentially infected clean wounds the incidence of serious (i.e., moderate or severe) infection was 19·2% (fig. 1). In the other clean wounds the incidence of serious infection was only 4·5%. The potentially infected clean wounds therefore had an infection-rate more than four times that of the other clean wounds. In all four types of charge infection was more common in the potentially infected wounds.



Infection in 673 clean wounds operated on in Edinburgh Royal Infirmary: *stippled*, trivial (redness at wound edge or stitch holes); *hatched*, moderate (signs of inflammation, including a little purulent exudate); *black*, severe (frank copious pus).

Discussion

Colebrook (1955) pointed out how few were the data on which to base an opinion on the incidence of infection in clean wounds, and he suggested that " it would be a salutary thing if one or two of our larger hospitals were to carry out a combined clinical and bacteriological follow-up of all their clean surgical cases over a period of, say, a year ". Similar views were expressed by *The Lancet* (1957).

We estimate that the incidence of serious infection in these 673 clean wounds from the Edinburgh Royal Infirmary during this three-month period in 1956 was 9·8%. There was an additional 16·3% of trivial infections, making a total of 26·1%. As has been said, we do not lay much emphasis on these trivial infections, because many of them may have been primarily due to stitch necrosis; and we prefer to focus attention on 9·8% serious infections. This is the average from four surgical charges—two general-surgery and two specialised charges. We

TABLE IV—INFECTION-RATES IN DIFFERENT HOSPITALS

Reference	Hospitals	Year	No. of wounds	Serious %	Trivial %	Total %
Meleney (1935)	Presbyterian Hospital, New York	1925	558	4·0	10·0	14·0
		1926	1132	4·0	11·0	15·0
		1933	1053	1·1	3·6	4·8
Howe (1954)	Massachusetts Memorial Hospitals, Boston	1953	429	4·6	2·5	7·2
Clarke (1957)	Bristol Royal Infirmary	1953	382	6·5	7·1	13·6
Present series	Edinburgh Royal Infirmary	1956	673	9·8	16·3	26·1

think it probable that the average would have been higher still if all six general-surgery charges of our hospital had been included in the survey, and not just the two of this study, because infection was much more common in the general-surgery cases.

Our survey covers a representative selection of the wounds of the public wards of the Edinburgh Royal Infirmary (there are no private patients), and the incidence of serious infection found in this series appears to be higher than that generally recorded. Complete comparison with other hospital series is impossible. In other series there is generally no mention of the criteria of assessment and no indication whether trivial infections have been included or not. The occasion, or time, after operation when the wound is inspected may have a bearing on the degree of infection discovered and recorded, but this is not commonly reported. The figures presented here refer to the most severe of the different degrees of infection which may have been observed for the same wound. Furthermore, realistic comparisons with the figures for other hospitals is impossible because the type of work done in these hospitals is unknown and may differ widely.

With these reservations in mind it is interesting to compare our results with certain studies where the criteria of assessment at least appear to have been similar to our own (table IV). The Edinburgh figures are seen to be higher, both for trivial and serious infection, compared with Meleney's (1935) pre-war series for the Presbyterian Hospital of New York, Howe's (1954) figures for the Massachusetts Memorial Hospitals of Boston, and Clarke's (1957) series for the Bristol Royal Infirmary.

The infection-rate in the Edinburgh Royal Infirmary is indeed a serious matter, and the surgeons and the board of management have taken cognisance of it and are improving the design and equipment of our operating-theatres. Apart from equipment and technique, the other factor responsible for our infections is the type of work done by our general-surgery charges. These charges have an abnormally high infection-rate because they deal with emergencies and accidents in addition to doing " cold " surgery. There are six general-surgery charges, each with its own operating-theatre, and one day a week they take it in turn to admit emergencies from a population of about a million. There is no separate accident service; therefore not only abdominal emergencies but also road accidents and fractures have to be admitted. Personal experience leads us to believe that accidental wounds are not particularly infectious, and an ischiorectal abscess or a ruptured appendix is more likely to infect other cases than is a road accident. However, the effect of a busy " waiting day " is to disrupt the sterility and efficiency of a " cold " operating-theatre.

We believe that the great majority of our infections originate in the operating-theatre, and that only a minority are cross-infections in the wards. We believe this because many of our operation wounds were left without any form of dressing cover and did not become infected subsequently in the wards; further, many of the infections were discovered on removal of the first dressing. Cross-infection, of course, is undoubtedly a serious risk to open wounds and burns.

It might seem that our system of transferring patients to convalescent homes a few days after operation could be partly responsible for development of infection. War-time experience of the danger of a long line of evacuation certainly supports this theory, but in point of fact our analysis did not bring this out. Indeed, very few wounds developed infection at a convalescent home or arrived seriously infected.

It is fair to say that, in spite of our high incidence of infection, the morbidity was relatively low, the mortality from sepsis was nil, and the main effect of the infections was to prolong the stay in bed in hospital. There were 35 deaths among the patients in this series, but in no instance was death attributable to infection from the wound. This was the opinion of the surgeons in the four charges, and it is pertinent to state that they also felt that this three-month period in the autumn of 1956 appeared to be a light one as regards sepsis. There were none of those devastating outbreaks in which every second wound seems to get infected. Similarly, Dr. R. E. Verney, physician in charge of nurses, pointed out that, although the staphylococcal carrier-rate in the nurses usually rose during the months of October–March, 1956 seemed to be an exception to this general experience.

It was originally hoped to follow up the wounds in the surgical charges over a complete year, but the labour of recording was found to be too heavy to be borne for this length of time. The main cause of the labour was that the patients were not kept in the same bed until the wound was finally healed. Many of the patients were transferred to convalescent homes a few days after the operation and even before their stitches were removed, and this entailed duplication of records and of observers. However, although the three-month period of this investigation is too short to give a wholly acceptable figure of the general incidence of infection in our hospital, we feel that it does provide a base-line; and we feel that the procedure of collecting the information that we have outlined has provided accurate figures for the four charges concerned. To lessen extra work for the ward staff, we hope to cover a complete year with a modified form of recording.

Summary

For a three-month period, October–December, 1956, all operation and accidental wounds in four surgical charges of the Edinburgh Royal Infirmary were carefully followed up.

Of 708 wounds, 35 were already seriously infected at operation and remained so. Of the other 673 clean wounds 60·5% were regarded as absolutely clean and 34·6% as potentially infected.

The incidence of serious infection in the 673 clean wounds was 9·8%. There was an additional 16·3% of trivial infections.

The two general-surgery charges showed the highest rate of serious infection (13·8%), the neurosurgical charge the next, and the orthopædic charge the lowest.

In comparing the infection-rates in different hospitals consideration should be given to the criteria of assessment of infection, the number of wounds that are potentially infected, and the type of surgical work done.

Possible sources of wound infection in the Edinburgh Royal Infirmary are discussed.

Acknowledgments are gratefully made to the surgeons, doctors, and sisters in the Royal Infirmary and the associated convalescent homes, who cooperated in this inquiry and kept their records with care and precision. The surgeons in charge of the four surgical charges were Prof. N. M. Dott, Prof. Sir Walter Mercer, Mr. T. McW. Millar, and Mr. W. A. D. Adamson. We also thank Dr. S. G. M. Francis and others of the administrative staff of the Royal Infirmary for their cooperation and assistance; Dr. J. H. Bowie for bacteriology and advice; Prof. J. H. F. Brotherston, of the department of public health and social medicine in the University of Edinburgh, for statistical facilities; and Miss A. Stephen for statistical calculations.

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THE UNFORGIVING MINUTE IN OBSTETRICS

Thoughts on Strategy and Tactics *

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ANTENATAL care, however diligent, has its limitations. It will be fruitless if, for example, the mother dies through delay in removing a retained placenta or the child is born dead because the practitioner, through lack of experience or want of confidence, has not applied forceps to terminate a second stage which lasted too long.

In obstetrics, as in battle, no amount of well-prepared strategy will avert defeat from a grave tactical error or from unimaginative failure to seize the unforgiving minute. Good antenatal care cannot be too strongly advocated, but to save a life in a tight corner something more may be needed.

In this country of late years administrative changes have fostered the idea that midwives, general practitioners, and consultants have separate and distinct roles. This has perhaps obscured the simple fact that they have one role in common—to practise skilled obstetrics whenever the occasion arises.

As to what in fact constitutes "skilled obstetrics" opinions can still differ considerably; and I shall therefore state my own views on some controversial situations.

PROLONGED PREGNANCY

Many, including myself, believe that a certain small number of stillbirths occur simply and solely because pregnancy has been allowed to go appreciably beyond the normally accepted span of 273–280 days. In primigravidæ prolonged pregnancy seems to be associated significantly with disproportion, and its management often resolves itself into dealing with this complication. In my opinion, whenever labour is 7–10 days overdue, the case should always be reviewed with a consultant.

In primigravidæ—particularly elderly ones—if the presenting part is high, and if there is some associated hypertension and the cervix is still unripe, surgical induction is unsuitable. Further delay must then become the full responsibility of the consultant.

In multigravidæ so-called ageing of the placenta is said to cause fœtal anoxia that may prove fatal before, or more commonly during, labour. This explanation is still contested; but at any rate it seems that a postmature infant is more likely to be stillborn if delivery is complicated by application of forceps or even by undue delay in the second stage followed ultimately by normal delivery. These are deviations that would not normally be disastrous to infants born at term. In a woman whose pregnancy seems to have continued well beyond its normal span, if the cervix is ripe, and the examining finger judges that artificial rupture of the membranes may easily be done, then it should be done. In these circumstances labour usually begins soon after induction, suggesting that the procedure has been correct and properly timed.

But I must say again that the alleged risks of postmaturity are still sub judice, and that some obstetricians think any interference essentially meddlesome.

PLACENTA PRÆVIA

A dozen years ago Macafee [1] pointed out that very many cases of placenta prævia can safely be treated conservatively in hospital until the pregnancy is well advanced, and that if this is done many more live infants will be born.

Cases of central or near-central placenta prævia are now being treated by cæsarean section; and the rules laid down by Sir George Makins [2] in the first world war for the treatment of secondary hæmorrhage seem particularly apt:

> "Direct ligature of the bleeding spot proved the safest and most effective method. . . . Forci-pressure and plugging both proved useful where direct ligature was impracticable, and formed the last resorts of surgery."

In the case of the uterus direct ligature implies emptying the uterus expeditiously, so that the normal living ligature mechanism of the interlacing musculature may have full and unrestricted effect on the uterine blood-vessels and sinuses. It has taken us rather a long time to learn that plugging of the vagina and pulling down a leg are essentially unsurgical and never likely to be widely successful.

PROLONGED LABOUR

Obstetric units vary considerably in their assessment of when true labour has become prolonged; but the old adage "never let the sun set twice on a labour" has a good deal to commend it.

The general practitioner carries a heavy responsibility in cases of prolonged labour. He often knows the background of the patient better than the consultant does, and in this type of case the advice of an experienced family doctor should seldom be rejected. Nor can a responsible general practitioner ever think much of the notion that "even if a woman does lose her first child she can always have another".

I may add that in these litigious days a husband is ultimately going to bring an action against a doctor for unnecessary and avoidable delay in bringing labour to an end—in a case where, for instance, the baby was stillborn or the mother died or developed a vesicovaginal fistula. The courts may yet agree to admit such a petition, though proof would undoubtedly be difficult.

RETAINED PLACENTA

Sheehan [3] has done much to focus attention on the true nature of so-called obstetric shock. He has shown convincingly the dangers of retained placenta and has urged removal after one hour. It is also important to remember that in some of these cases, even in the absence of severe

* Extracts from a lecture given to the Liverpool Medical Institution in 1956.

1. Macafee, C. H. G. *J. Obstet. Gynaec., Brit. Emp.* 1945, **52**, 313.
2. Makins, G. H. History of the Great War: Medical Services Surgery of the War; Vol. II, p. 181. H.M. Stationery Office, 1922.
3. Sheehan, H. L. *Lancet*, 1948, i, 1.

bleeding, the patient deteriorates merely because the placenta is still within the uterus. (Not everyone agrees with this.)

Anæsthesia for manual removal of the placenta should be light. There is great danger in inducing deep anæsthesia for a forceps delivery, and perhaps again a little later in a vain attempt to express the placenta by Credé's method, and maybe yet a third time, after several hours, for manual removal of the placenta. This can be disastrous.

Any obstetrician—consultant or practitioner—who embarks on a forceps operation should be technically prepared to go on to remove the placenta. There is much to be said for coincident manual removal of the placenta immediately after the forceps extraction, during the same anæsthesia, unless the placenta can be readily expressed after the routine intravenous administration of ergometrine.

BREECH PRESENTATION

At least some of the bad results obtained outside hospital in cases of breech presentation are due largely to insufficient help and poor anæsthesia. To perform a breech extraction comfortably, one needs plenty of good assistance, a competent anæsthetist, proper surgical anæsthesia, a nurse assistant, and a generous episiotomy. Given these, with careful antenatal assessment of fœtal size and routine X-ray pelvimetry, breech delivery loses quite a few of its fears. But a fair proportion of primigravidæ—possibly 12%—will require elective cæsarean section.

The use of external version under anæsthesia is debatable. Occasionally a stillbirth results from this manœuvre; and if, besides the abnormal presentation, there are any subsidiary reasons why the uterus might be emptied abdominally as a precaution, then it certainly seems unwise to attempt an antenatal procedure that is itself known to carry some risk of placental separation.

CÆSAREAN SECTION

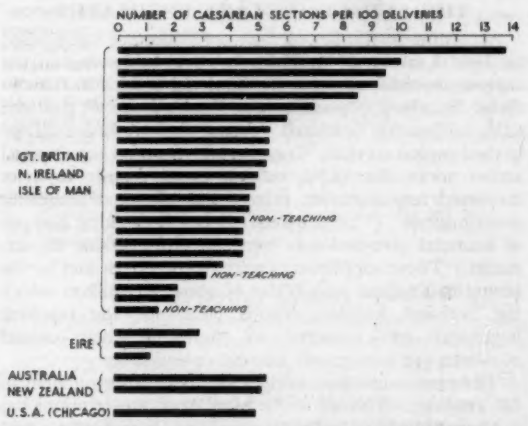
Here I show, in the table and figure, the cæsarean-section rates from several teaching hospitals in Great Britain, the Commonwealth, Eire, and the United States of America. These are a matter of importance not only to the consultant obstetrician but also to the general practitioner; for, when he is in sole charge of his patients at the onset of labour, he is the person who does or does not take steps to initiate the operation.

INCIDENCE OF CÆSAREAN SECTIONS

	Marshall [4] 1943–47	Corbett 1951–55
No. of deliveries	125,179	329,822
No. of cæsarean sections	7,762	16,472
Incidence	6·2%	5·0%

A 5% yearly cæsarean-section rate represents a very slight downward trend in comparison with the figure given in the survey made almost ten years ago (Marshall 1949). That survey covered far fewer hospitals than does the present one. If the figures for Marshall's group of hospitals for 1951–55 were extracted from the present figures they would show a yearly section-rate of 6%—i.e., no change since the period 1943–47.

On indifferent judgment and inadequate clinical sense may well depend the bad odour in which cæsarean section is often held. A speaker at the 1955 conference on general-practitioner midwifery convened by the College of General Practitioners [5] referred to it as a " dangerously safe " operation. What he probably meant was that it was often done unnecessarily and too lightheartedly, and that, like every other abdominal operation, it carries some risk. Certainly, if it is done too late in labour, the risk is greatly increased. The danger, I think, really lies in prolonging labour beyond reasonable limits.



Yearly cæsarean-section rate (i.e., average yearly rate for 1951–55) as percentages for 30 hospitals, mainly teaching.

Imprudent deferment of cæsarean section causes a steep rise in the risks of postoperative peritonitis. Bell,[6] in a recent paper to the South African Obstetrical Society, made the following statement:

" In reviewing the present position of cæsarean section it is satisfactory to note that Marshall's paper (1949) was not followed by a wild orgy of sections as predicted by some of those who joined in the discussion of his paper. My own memory recalls more women on whom I regret not doing a cæsarean than those where the operation might have had slender indications."

Cæsarean-section rates vary, sometimes greatly, from one centre to another. No consultant obstetrician can allow his judgment continually to be impeded by having to keep his section-rate " respectably " low. He must on each occasion follow what seems to be the proper course and must accept responsibility whenever the need arises. Quite clearly no such thing as an orgy of cæsarean sections will ever take place, and the rates must vary in different centres for reasons that are for the most part obscured in formal reports.

OBSTETRIC ANÆSTHESIA

In 1956 the *British Medical Journal* [7] drew attention to the alarming frequency of deaths under anæsthesia, and to their relative frequency in the practice of midwifery. The dangers of inhaling vomit have always been known, but Jeffcoate's [8] observation that " in forceps delivery the use of general anæsthesia represents a greater hazard than the obstetrical manœuvre " stands out with disquieting prominence and arresting clarity. There seems little reason to doubt that, in general-practitioner midwifery, chloroform is still fairly widely used. Is it sufficiently realised in our profession that, for operative vaginal delivery, local anæsthesia offers an always safer and often better alternative to the general anæsthetic?

Grateful acknowledgment is made of the kindly cooperation of friends and colleagues in this country and abroad who have supplied material from which the statistics cited here have been compiled.

4. Marshall, C. M. XIIth British Congress of Obstetrics and Gynæcology: Introductory Papers, 5. 1949.
5. Supplement to the college's *Newsletter* no. 10, p. 28.
6. Bell, A. Personal communication.
7. *Brit. med. J.* 1956, ii, 868.
8. Jeffcoate, T. N. A. *ibid.* 1953, ii, 951.

THE SUPPLEMENTARY ESTIMATES

According to the Supplementary Estimates [1] published on Feb. 4, about £9 million more will be needed in the current financial year for the National Health Service in Great Britain (£7½ million for England and Wales and £1½ million for Scotland). About half this sum will go to the hospital services. Together, the hospital boards need rather more than £5½ million extra, mainly to meet increased remuneration, prices, and National Insurance contributions. (The last item offers a fascinating glimpse of financial give-and-take between Government departments.) These supplements are to some extent met by the saving in England and Wales of about £1 million which the regional hospital boards (but not the teaching hospitals) are expected to show on their capital accounts.

The pharmaceutical services will need a supplement of £2½ million. The fall in the number of prescriptions has not been sufficient to offset the higher average cost per prescription, and it has also meant a shortfall in payment by patients in England and Wales of £1,099,000. In the estimates for England and Wales an extra £380,000 is provided for the purchase of poliomyelitis vaccine from Canada and the United States.

The Ministry of Health itself has a supplementary estimate for £405,000. The National Milk scheme needs an extra £1,150,000, but this is almost offset by an expected saving of £1,130,000 on other welfare foods. The extra money needed by the milk scheme is said to be due to the fact that people are using more liquid milk instead of National Dried Milk.

Public Health

RESPONSE TO POLIOMYELITIS VACCINATION

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CHILDREN in Iceland were vaccinated against poliomyelitis in the autumn of 1956. American vaccine injected subcutaneously and Danish vaccine injected intradermally were used at the same time in the same localities.

This gave an opportunity for measuring antibody in comparable groups of children after both types of vaccination. The effects of the two methods were compared by means of a survey in two villages, and an unexpected difference was found between the responses of the children in the two outwardly similar localities, irrespective of whether they had received the American or the Danish vaccine.

A brief explanation of recent poliomyelitis history in Iceland is needed to put our findings into focus.

In 1955 an extensive epidemic of type-1 poliomyelitis had spread over Iceland as shown in fig. 1, which is based on measurements of type-1 antibody in children after the epidemic. The distribution of type-1 antibody agrees well with the distribution of reported clinical cases in 1955 with two exceptions.

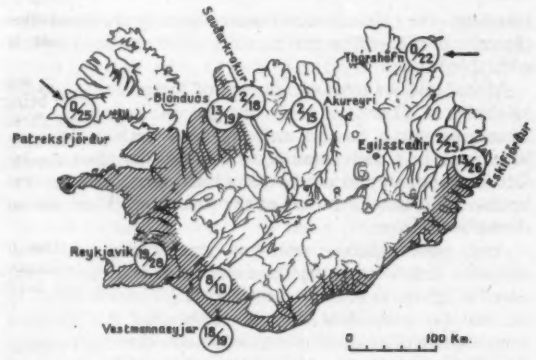

Fig. 1—Map of Iceland showing area involved in 1955 poliomyelitis epidemic (hatched). Figures show number of children with type-1 antibody out of number tested in various areas.

There had been outbreaks of Akureyri fever (epidemic neuromyasthenia) (Sigurdsson et al. 1950, Poskanzer et al. 1957) in two small towns, Patreksfjördur and Thórshöfn (indicated with arrows on the map), outside the type-1 epidemic area during and after the poliomyelitis epidemic (table I). These outbreaks were provisionally *registered* as poliomyelitis, though it was recognised from the beginning that they were not poliomyelitis but Akureyri fever. This diagnosis was supported by the fact that poliovirus could not be recovered from these cases. No antibody to type 1 was found in children in these two communities after the outbreaks (out of 25 children in Patreksfjördur and 22 in Thórshöfn). This is a clear indication that these outbreaks were not caused by type-1 poliomyelitis virus.

The other discrepancy between the distribution of registered cases and the distribution of type-1 antibody in children after the outbreak is that antibody was found in three localities—Blönduós, Vestmannaeyjar, and Eskifjördur—on the fringe of the epidemic area, though no clinical disease had been reported there.

TABLE I—REGISTERED CASES OF AKUREYRI FEVER IN PATREKSFJÖRDUR (1382 INHABITANTS) AND THÓRSHÖFN (780 INHABITANTS)

—	—	1955			1956			
		Oct.	Nov.	Dec.	Jan.	Feb.	March	April
Patreksfjördur	non-paralytic ..	2	27	35	32	9	3	0
	paralytic ..	0	9	10	6	2	0	0
Thórshöfn	non-paralytic ..	0	0	10	30	28	11	17
	paralytic ..	0	0	1	9	7	1	0

Investigation

A survey of antibody to all three types in children under 10 years of age was carried out before vaccination was begun. On the basis of that survey it was decided to test the efficacy of the two types of vaccine in children in two communities outside the area of the 1955 type-1 poliomyelitis epidemic, Thórshöfn and Egilsstadir, in the North East of Iceland.

In Thórshöfn (a district with 780 inhabitants), from December, 1955 to April, 1956, 18 paralytic cases and 96 non-

TABLE II—ANTIBODY IN CHILDREN UNDER 9 YEARS, BEFORE VACCINATION

—	No. of children	No. with antibody to type		
		1	2	3
Thórshöfn	22	0	1	5
Egilsstadir	25	2	0	6

1. 1957-58 Supplementary Estimate. Civil Estimates and Estimates for Revenue Departments. H. M. Stationery Office. Pp. 179. 11s. 6d.

paralytic cases of Akureyri fever had been registered. This is an incidence of 14·6%. But, as table II shows, the prevaccination poliomyelitis antibody status was in fact very similar in Thórshöfn and Egilsstadir.

Only children without detectable previous antibody to any type were included when the results of vaccination were being tested. About half of the children in each place were inoculated with Danish vaccine and the other half with American vaccine. Fig. 2 shows the titres observed in the children two months after the second injection of American or Danish vaccine. The two types gave comparable rise in titre after the second injection, but the results were rather poor on the whole.

The interesting fact emerged, however, that the rise in antibody titre differed much according to the place of residence, irrespective of whether Danish or American vaccine was used. Fig. 3 shows that there was only a slight rise in antibody to type 3 and type 2 in Egilsstadir but a relatively good rise in Thórshöfn. We have tried to look for extraneous factors,

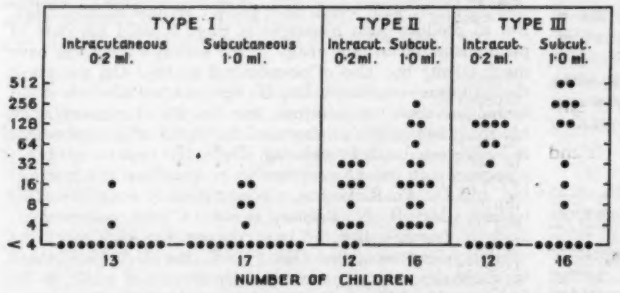

Fig. 2—Titres in 30 vaccinated children after second injection.

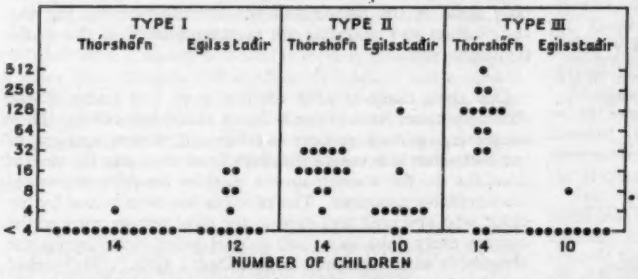

Fig. 3—Titres after second injection in Thórshöfn and Egilsstadir.

connected with the vaccination, which might explain the different response in the two groups of children. We have found no such explanation, and we assume now that the difference lies in the children themselves, or in other words that the children in the two localities varied systematically in their responsiveness to vaccination with type-3 and type-2 poliovirus.

We report this to suggest that other factors than detectable prevaccination level of poliomyelitis antibody may influence the response of a given population to vaccination, and that perhaps previous immunological experience with Akureyri fever may be such a factor.

Summary

The responsiveness of children to vaccination against poliomyelitis varied greatly in two separate localities in Iceland.

In one isolated locality, without previous history of poliomyelitis, antibody rise to all three types was extremely poor. In another isolated locality the response to types 2 and 3 was much better. This second locality had recently suffered a severe outbreak of Akureyri fever.

This experience seems to suggest that other factors than a detectable level of antibody may influence the response of a given population to poliomyelitis vaccination.

The remarkably good antibody response after Salk vaccination often observed in children without previous antibody might perhaps in some cases be explained by the existence of basic immunity acquired through a related infection.

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Acute Respiratory Disease in Babies

The Ministry of Health reports that since Jan. 20 an increase has been observed in the number of babies in London needing admission to hospital. Since that day between a third and a half of all admissions arranged by the Emergency Bed Service on account of acute respiratory illness has been of children under 5, and of these most have been from 3 months to 2 years old. There has been no corresponding increased need for hospital beds for older patients. There are indications of a similar situation in Birmingham.

The babies usually have a history of a cold for two or more days followed by deterioration, often rapid, with evidence of disease of the lower respiratory tract. The more severely ill children have been restless and cyanosed and have shown intercostal recession on inspiration and other evidence of respiratory-tract obstruction, but signs of consolidation have not been prominent. There have been few deaths. In many cases oxygen therapy has been essential, whereas antibiotics do not seem greatly to have affected the course of the illness though they may have helped to avert secondary infection. No evidence has been obtained to suggest a bacterial cause.

In November, 1953, outbreaks resembling the present one were observed in London, Liverpool, and Manchester,[1] and another outbreak in Sunderland in 1953 [2] seems very similar. Efforts to show that the illness was due to influenza or other viruses were unsuccessful, and the ætiology is still unknown. Additional information might be obtained if outbreaks were reported to medical officers of health as soon as they were recognised.

Clean Air Act

Some provisions of the Clean Air Act are already in force—e.g., powers enabling local authorities to establish smoke-control areas. One of the stumbling-blocks in certain areas—the reluctance of coalminers to buy smokeless fuel when they receive free concessionary coal [3]—has been overcome by the National Coal Board's agreeing to buy back concessionary coal from any miners whose home is in a smoke-control area.

By order of the Minister of Housing and Local Government, the remaining provisions of the Act will come into force on June 1. Under these provisions the emission of dark smoke from chimneys will be banned and emission of grit and dust minimised. A fine of up to £100 will be the penalty for the emission of smoke darker than shade 2 on the Ringelmann chart. This ban applies to all chimneys, but domestic chimneys rarely exceed shade 2. Certain defences are allowed—that suitable fuel was unobtainable, that a furnace was being lit from cold, or that the apparatus had failed unforeseeably. All practicable steps must be taken to minimise the emission of grit and dust from existing furnaces (except small domestic

1. Ministry of Health: Annual Report of the Chief Medical Officer, 1953; p. 45.
2. Haycock, J. B., Noble, T. C. *Brit. med. J.* 1956, i, 438.
3. *Times*, Jan. 18, 1958.

boilers), and all new large furnaces will have to be equipped with plant, approved by the local authority, to arrest grit and dust.

Progress with Detergents

In some places masses of foam floating on rivers and canals are as familiar a sight as advertisements for detergents are everywhere; and one town has complained of foam from a weir blowing along its streets. This is not only spectacular but also possibly dangerous because masses of foam seriously reduce the chances of rescue if anyone falls in the water. The Standing Technical Committee on Synthetic Detergents, set up in January, 1957, has now issued a progress report,[1] in which it points out that the rapid increase in the use of surface-active material has levelled off since 1953; in 1956 the United Kingdom figure was 41,000 tons, of which 34,500 tons was used in the home.

The committee is considering the effects of detergents on the essential aeration processes at sewage works and the effects on the effluent of antifoaming agents used there. The Water Pollution Research Laboratory is investigating the toxicity of detergents to fish.

The committee is satisfied that the manufacturers are seriously trying to overcome the disadvantages of their products by finding a substitute that can be readily eliminated by the present sewage methods.

The Registrar General's Civil Tables

The Registrar General has issued the second volume [2] of his review for 1956.

The marriage-rate was 15·7 per 1000 population (16·0 in 1955); more than a fifth took place in March, doubtless for fiscal reasons. In the 352,944 marriages, 30,844 men and 113,494 women were under 21 years old. The commonest age for marriage remained 23 for men and 21 for women. The birth-rate (15·6 per 1000) was the highest since 1950; illegimate live births were 4·8% of all live births (4·7% in the previous three years). There were 700,355 live births; 8660 confinements resulted in twins, 78 in triplets, and 1 in quadruplets. The number of new petitions filed for divorce increased from 28,314 in 1955 to 28,426, the first rise since 1951; the average number in 1951–55 was 32,168.

Medicine and the Law

Guilty but Insane

THE Homicide Act, 1957, introduced the defence of diminished responsibility in order to provide for cases where the mental condition of the accused does not amount to insanity as defined in the McNaughten rules. In general, it will no doubt be easier to prove diminished responsibility than insanity. The McNaughten rules remain in force, however, and there may be cases in which the nature of the medical evidence is such that a plea of insanity will be the more appropriate defence. In other words, the legal definitions of insanity and diminished responsibility involve a difference of kind as well as degree.

The McNaughten rules were in fact applied in a murder trial at Leicester Assizes last week, in which a man aged 24 was charged with the murder of an 8-year-old boy. Medical evidence was given that the accused was suffering from schizophrenia and did not know at the time that his action was wrong. He was found guilty but insane.[3]

1. Ministry of Housing and Local Government: Progress Report of the Standing Technical Committee on Synthetic Detergents. H.M. Stationery Office, 1958. Pp. 8. 6*d*.
2. Registrar General's Statistical Review of England and Wales for the Year 1956. Part II: Tables, Civil. H.M. Stationery Office, 1958. Pp. 180. 7*s*. 6*d*.
3. *Times*, Feb. 4, 1958.

In England Now

A Running Commentary by Peripatetic Correspondents

FOR a great part of mankind, some kind of creative activity is essential for a satisfying life. Many men and women, however satisfying their professional work may appear, cannot rest unless they produce works of art as well, and painting is a tranquilliser shared by many, including heads of States and doctors. Tranquillity is the keynote this year at the Medical Art Society,[1] as Sir Philip Manson-Bahr's *Cologne Cathedral*, Dr. E. J. E. Topham's *Isleworth*, and Dr. Isabel Wilson's *Clifton Bridge* exemplify. Mr. R. T. Payne's *Nude* is a very pleasing and simple composition, while Dr. T. Anderson's water-colour *Orchard, Impington* is tranquil but also one of the most original and lively pictures in the show.

Such a spark of liveliness is a feature much missed in most of the pictures. Anyone lucky enough to have seen the recent film of Picasso at work must have been impressed by the deceptive ease with which each picture seemed to be created. But to produce such masterpieces there is need not only of phenomenal talent (and many of the society's members have much talent) but also of phenomenal vitality. On the whole the sculpture—especially Dr. G. Konstam's *Fallen Horse*—is more vital than the paintings, but Dr. Ph. Tuttnauer again has some fine individual canvases that speak of an exuberance to be expressed only by painting. Dr. Sylvia Payne contributes a portrait that, though unattractive, is disturbing and interesting, and Dr. G. E. Loxton a flower-piece of notable surface texture. Mr. B. N. Brooke, besides a bold water-colour, *Lock at Lapwith*, has the most outstanding picture of the exhibition—an oil called *Calvary*. In the dark background are three dry empty crosses near the summit of a hill; in the foreground unfold two heavy succulent plants, one apparently still in the ground, the other uprooted and drifting. One can only guess at the meaning of the symbolism here; but the composition and colouring are as accomplished as the whole picture is vital.

* * *

Our chest clinic is held twice a week and many of our African patients attend from as much as 200 miles away. They are treated on P.A.S. powder and isoniazid tablets, and one of our difficulties is to ensure that back home they take the correct dose, for the flat wooden spoons used by the African peasant are unreliable measures. The problem has been solved by my chief, who observed that even in the most remote parts of the country every duka, as a small shop is called here, carries the ubiquitous advertisement, "Drink Dash's Cola". He worked out that 5 g. of P.A.S. fills two bottle-tops with the corks removed. So our prescription runs "2 flat Dash's Cola tops P.A.S. powder twice daily."

* * *

I have had an experience which I believe to be unique. On a Monday morning, when I should have been in the wards, I drove to the Royal College of Physicians, wearing pyjamas and sandals and with my hands as black as the ace of spades. It was my husband's final viva in the M.R.C.P. examination and the circumstances were extenuating.

After leaving him at the door of the college my problem was how to pass the time. At first I sat shivering in the car beside a No Parking notice. The icy January wind came through the floorboards and caught my pyjamas. I was still suffering from this when a policeman, apparently not interested in pyjamas, asked why I displayed last year's licence. No sooner had I finished explaining than another policeman appeared and I had to explain all over again. I decided that, pyjamas and all, I would have to leave the car and hope for the best about the No Parking notice and last year's licence.

My pyjamas were rather gay, so I brought a curl down over my forehead, decided that I would pass for an art student, and walked towards the National Gallery. On the way I passed two characters whom I thought looked even queerer than I

1. The exhibition is on display at Walker's Galleries, 118, New Bond Street, until March 5.

did, and this gave me the confidence to run up the steps and through the swing doors. Once inside I felt less sure of myself. It looked so formal, including the arty-ladies selling postcards. There were other people, presumably real art students, with curls over their foreheads, but none had hands as black as mine or wore pyjamas. However, my confidence rose when no-one stared at me, not even the custodians. Obviously this was an everyday occurrence. I even managed to forget my plight for a while and to enjoy some of my favourite pictures.

By the time I thought my husband might be reappearing I felt almost normal and able to face a walk in Trafalgar Square. Near one of the fountains some people stared at me rather offensively, but these, I decided, were tourists in search of local colour. Increasingly confident, I walked happily up the west side of the square and peered in at the windows of the college to see if I could see my husband in the moment of agony. There was only a man polishing a table, but when I turned round, there, coming towards me, inescapably staring at my pyjamas, my hands, and my curl, was my Chief. To give him his due, he gave me a sort of sickly smile.

* * *

Last week my hand lighted on an unfamiliar volume erupted in the domestic spring upheaval, a treatise on tobacco-smoking sent for review in 1911 when I was editing my hospital journal. It is a depressing work—even to a non-smoker. Its gloom is illuminated by a solitary ray of humour, and that unintentional. As "*corrigendum:* page 56, for *salvation* read *salivation.*"

The author traced a more or less direct connection between Sir Walter Raleigh's discovery and his disastrous termination. The "so-called soothing weed" was credited with the production of tabes and sterility, for "even the perspiration of a smoker being absorbed by his wife can poison the ovum." The opinion was advanced that the only women who suffer from cancer were the wives or daughters of men who had indulged in tobacco to excess. (To appreciate these views at their full value it should be added that the author was a doctor.)

After these charges, the inclusion of insanity was a modest expectation. Yet I visualised the smoker-reader grinning as he lighted his pipe with a spill from one of the pages, and concluding that so far from tobacco-smoking leading to insanity, there would appear to be abundant evidence that this infirmity results from its abstinence.

* * *

I agree with last week's correspondent that many "insomniac" patients are trying to get too much sleep. I was once called to one who was lying in bed at 4 p.m.

"What's the trouble?"
"I want some sodium amytal."
"Can't you sleep?"
"No."
"What time do you go to bed at night?"
"Oh, I sleep all right at night; it's in the daytime I have trouble."

* * *

A case-record received in the office the other day told of a child that was born with "hypertelevision". Is this another example of a throwback or just plain ATV-ism?

* * *

In each of us there is an inborn urge to feed birds and animals, an urge that makes us scatter bread to sparrows and to ducks, brings business to the dried-pea vendors at Trafalgar Square, encourages dogs and polar bears to sit up and beg, and leads to occasional warnings at London Zoo that certain animals ought not to be fed.

There is a little courtyard in the Inner Temple where a fountain plays (when not afflicted with stricture), where lawyers stroll, or sit and munch sandwiches, and where a perambulator, containing a sleeping infant, carries the placard:

PLEASE DO
NOT FEED
FIONA

Letters to the Editor

NEW LOOK IN RESPIRATORY INFECTIONS

SIR,—My purpose is to draw attention to changes in the pattern of chest infections seen this winter in the medical wards of a general hospital—changes which were sudden and unexpected.

The rush of chest cases following on the much-publicised Asian flu did not materialise, and the first intimation that anything was amiss was when a male, age 54, being treated in hospital for diabetic neuritis died in three days, and at necropsy the cause of death was an acute staphylococcal pneumonia. This occurred in October, and although there were 3 more staphylococcal pneumonias admitted in this month, 1 of which was fatal, the real blow did not fall until November and December when 22 patients suffering from staphylococcal pneumonia were treated in my wards. The lung infection was so acute and severe that erythromycin or novobiocin was given at once in suspected cases (especially if the sputum was a dirty brown-green colour and non-aerated) without waiting for the laboratory report. In this way lives were saved.

The clinical picture of the emphysematous patient was that of an acute bronchiolitis with mental disturbance; they were severely cyanosed and there were surprisingly few physical signs in the lungs.[1] It was not surprising, therefore, that tracheostomy and suction did not relieve the cyanosis in one patient, and, following this experience, when an older emphysematous patient, aged 72, presented in the same way with extreme cyanosis and semi-coma, we hesitated to advise tracheostomy although his chest was "bubbly" and he could not raise his sputum. Instead, we gave erythromycin and within forty-eight hours he was conscious and fairly well oxygenated.

In spite of these experiences, the staphylococcus outwitted us in January of this year when it manifested itself as a classical lobar pneumonia in a woman of 32. She died, and in retrospect the anomalous feature was the abundant rales in the affected lung at the height of the illness.

The sputum was examined in 62 patients who were admitted to my wards with a chest infection between September, 1957, and January, 1958, inclusive. 42 also had chronic bronchitis and emphysema and of these 13 died; 4 of the remainder died. Initial examination of the sputum showed non-pathogens in 29, pneumococci in 10, hæmophilus in 10, coliforms in 9, and *Staphylococcus pyogenes* in 11. Subsequent sputum examination of the same patients showed 4 more with hæmophilus, 4 with pneumococci, and 15 with *Staph. pyogenes.* Only 5 of the staphylococcol strains grown were penicillin-sensitive, and 3 patients who had *Staph. pyogenes* in the sputum were clinically well. Erythromycin and novobiocin proved to be the most effective drugs against the *Staph. pyogenes;* although mycelia of monilia were found in the sputum of treated cases, they disappeared spontaneously.

The male patients were nursed in six-bedded wards, and although cross-infection was never proved it was strongly suspected.

It may be that the notifiable infectious disease of the future will be *Staph. pyogenes* pneumonia and use may again be found for our empty infectious-disease hospitals.

One advantage of a personal bronchitis and emphysema clinic, such as I run, is that patients may be admitted to hospital earlier in their infection, but this did not prevent 2 of my patients dying before admission.

At our peril will we trust or ignore the staphylococcus, which may use different disguises to deceive us; the other pathogens in the respiratory tract do not appear to

1. Simpson, T. *Brit. med. J.* 1954, i, 297.

be so cunning. We should reassess the value of prolonged antibiotic therapy in the chronic bronchitic. Nature may not submit to our attack—her mood now is certainly ugly and has left us licking our wounds. Let us hope her anger is spent.

Chase Farm Hospital,
Enfield, Middlesex. THOMAS SIMPSON.

THE LIFE FOR ME

SIR,—Dr. Richard Cobbleigh's accounts of his progress through the medical jungle are always stimulating reading, the more so as not all of us would agree with his diagnosis of what are false trails and blind ends. Even his myths (such as the one in his Widdicombe letter of Feb. 8—the "M.O.H. who *still* doesn't believe that G.P.s exist") throw some light, though only scanty illumination, on some obscure professional mental processes which perhaps merit more study from his newly adopted specialty than they have yet received.

Apparently hydrocortisone ointment as a panacea for skins lets us all be dermatologists. It is not quite so clear whether E.C.T. as a panacea for mental illness lets us all be psychiatrists, but I hope that as the Cobbleigh Career progresses in this field it will encounter the growing edge which deals with prevention. Not a few of his new colleagues have passed beyond empirical treatments like E.C.T. to cope with the more difficult problems of trying to find the psychological factors leading to problem families, juvenile delinquency, neurosis, and behaviour problems. And if our Angry Young Doctor-turned-psychiatrist ventures this far he may even once again find himself back in "those Clinics" where the M.O.H. has already extended a warm welcome and an attentive ear to preventive psychiatry.

I look forward eagerly to Dr. Cobbleigh's reflections on his further progress.

Public Health Department,
London, S.E.1. J. A. SCOTT
Medical Officer of Health for the
County of London.

BETWEEN GUESSWORK AND CERTAINTY IN PSYCHIATRY

SIR,—I agree most profoundly with Professor Lewis's contention (Jan. 25) that, in certain directions, progress in psychiatry requires collaboration between psychiatrists and psychologists. Speaking as a person trained in both disciplines, I would like to draw attention to certain mutual irritations which keep the two professions apart. By and large, psychologists are more research-minded than psychiatrists and have a better grounding in scientific method, and especially in statistics. Speaking for the moment as a psychologist, I would record with deep feeling the fury which psychiatric colleagues can arouse by their ignorance of the significance of a simple statistical technique which should present no challenge to the intellect of anyone who has passed G.C.E. mathematics at O level. Therefore, if psychiatrists are to be acceptable colleagues to psychologists they must at least learn some simple statistics.

If I may now switch to my alter ego, the psychiatrist, he points out that the psychiatrist is more pragmatic than the psychologist. Pragmatic is, to him, a more polite term for "not up in the clouds". The psychiatrist wants techniques which will work in the clinical hurly-burly of wards and outpatient departments. He has no love for the irritating psychologist who keeps telling him that his pet methods have never been scientifically validated, but never seems to offer an alternative which can be vouched for by science.

It should not be beyond the united resources of the two professions to solve this little problem in interpersonal relationships.

Long Grove Hospital,
Epsom, Surrey. A. B. MONRO.

DUODENAL ULCER: AN OBSERVATION

SIR,—Data from several sources have shown an association between blood-group O and duodenal ulcer. Cumulative figures have been weighted to confirm this association in a manner appropriate to the varying incidence of blood-group O in the differing communities from which material has been drawn. The object of this letter is to draw attention to a phenomenon which appears if ABO blood-group data in subjects with duodenal ulcer are compared with control blood-group data from the same place, counting each observation as a separate and equivalent unit.

TABLE I

Place	Source	$\frac{A}{A+O}$ Ratio	
		Control	Duodenal Ulcer
London	Aird et al.[1]	0·480	0·368
Newcastle	Aird et al.[1]	0·443	0·363
Manchester	Aird et al.[1]	0·454	0·425
Denmark	Køster et al.[2]	0·520	0·433
Glasgow	Peebles Brown et al.[3]	0·375	0·348
Iowa	Buckwalter et al.[4]	0·476	0·404
Liverpool	Clarke et al.[5]	0·444	0·342
Norway	Westlund & Heistö [6]	0·569	0·470

The A/A+O ratio in controls and of macroscopically proven cases of duodenal ulcer from previously published data are shown in table I and presented graphically in fig. 1. There is a significant correlation between the A/A+O ratio of duodenal ulcer subjects and the A/A+O ratio of the control populations

1. Aird, I., Bentall, H. H., Mehigan, J. A., Roberts, J. A., F. *Brit. med. J.* 1954, ii, 315.
2. Køster, K. H., Sindrup, E., Seele, V. *Lancet*, 1955, ii, 52.
3. Peebles Brown, D. A., Melrose, A. G., Wallace, J. *Brit. med. J.* 1956, ii, 135.
4. Buckwalter, J. A., Wohlwend, E. B., Colter, D. C., Tidrick, R. T., Knowler, L. A. *J. Amer. med. Ass.* 1956, **162**, 1215.
5. Clarke, C. A., Cowan, W. K., Wyn Edwards, J., Howel-Evans, A. W., McConnell, R. B., Woodrow, J. C., Sheppard, P. M. *Brit. med. J.* 1955, ii, 643.
6. Westlund, K., Heistö, H. *ibid.* 1955, i, 847.

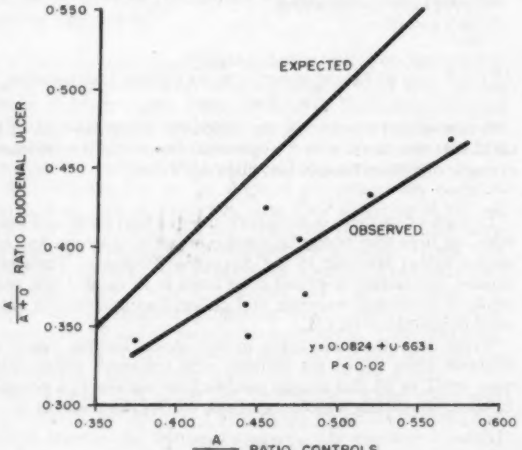


Fig. 1—Duodenal ulcer: A/A+O ratio compared with controls from 8 sources.

TABLE II

Place	Source of control blood-group data	Control blood-group-A gene frequency	Duodenal ulcer crude male mortality age 60–69 (1951–53)
Norway	Heistö [7]	0·322	3·6
Denmark	Køster et al.[2]	0·283	13·6
U.S.A.	Hogg and Pack [8]	0·258	18·0
Australia	Simmons et al.[9]	0·243	20·3
Scotland	Peebles Brown et al.[3]	0·195	34·2

($r = 0{\cdot}823$, $P < 0{\cdot}02$). The position of the regression line shows the association between blood-group O and duodenal ulcer. More interesting is the observation that the association with blood-group O in duodenal ulcer increases as the proportion of blood-group A in the controls increases ($\chi^2 = 28{\cdot}78$, $N = 7$, $P < 0{\cdot}001$).

One possible interpretation of this phenomenon is that the possession of blood-group A protects against duodenal ulcer, and as blood-group A increases in control populations there is selection against blood-group A in corresponding duodenal-ulcer populations.

If such selection does occur, one might expect that with the varying prevalence of blood-group A between different populations, there would also be a reciprocal variation in the prevalence of duodenal ulcer. Direct prevalence figures are difficult to obtain, but crude mortality-rates, with their limitations, are available. As duodenal ulcer is a predominantly male disease, with the greatest number of deaths between 60 and 70 years, it appears reasonable to compare crude mortality-rates in men of this age-group rather than standardised mortality-rates, provided that the standard of death notification in communities to be compared is also comparable. From the figures provided by the World Health Organisation [10] for the years 1951–53 inclusive, the mortality-rates for Australia, Scotland, the United States, Denmark, and Norway can be used. Comparison with ABO blood-group distributions will be valid only provided that within each country there are no wide variations in the ABO blood-group frequencies, and for this reason data from England and Wales cannot be included. From the blood-group data of the countries cited, blood-group-A gene frequencies have been calculated by the method of Dobson and Ikin,[11]

7. Heistö, H. (1956), quoted by Sørensen, K. H. *Danish med. Bull.* 1957, **4**, 45.
8. Hogg, L., Pack, G. T. *Gastroenterology*, 1957, **32**, 797.
9. Simmons, R. T., Semple, N. M., Graydon, J. J. *Med. J. Aust.* 1951, i, 105.
10. *Epidem. vit. Stat. Rep.* 1955, **8**, 398.
11. Dobson, A. M., Ikin, E. W. *J. Path. Bact.* 1946, **58**, 221.

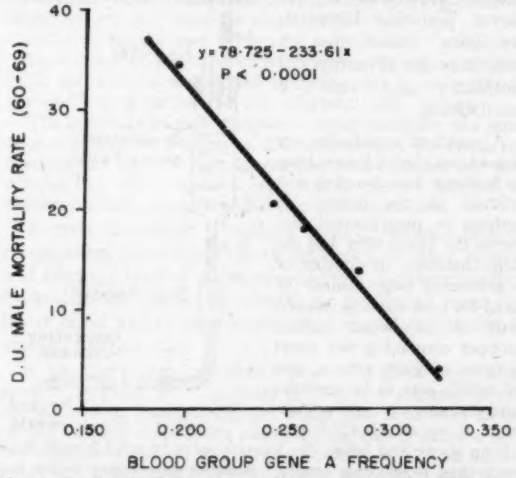


Fig. 2—Duodenal ulcer: crude male mortality at age 60-69 from 5 sources as a function of the prevalence of blood-group-A gene in a control population.

and when they are compared with the selected male mortality-rates from duodenal ulcer (table II, fig. 2), an excellent negative correlation exists ($r = 0{\cdot}992$, $P < 0{\cdot}0001$).

The data will support the hypothesis that blood-group A protects against duodenal ulcer, provided that the inheritance of the disease is not related to ABO blood-groups, and this appears to have been established by Clarke et al.[12] It has been shown with gastric diseases [13 14] that the association with ABO blood-groups appears to be related to intragastric site, irrespective of the nature of the disease, and it seems likely therefore that the association between duodenal ulcer and blood-group O may be a similar manifestation of site-susceptibility.

From the work of Hartmann [15] the secretor status of an individual appears to determine the amount of blood-group substance present in the duodenal mucosa. If blood-group-A substance gives best protection against duodenal ulcer, it would be reasonable to expect that where less material is present there would also be less protection, and this may explain why Clarke et al.[12 16] show an excess of non-secretors in subjects with duodenal ulcer. These workers hold that blood-group and secretor status are not independent factors in the genesis of the disease, and this receives support from the data of McConnell and Sheppard [17] where the variations from the control ABO blood-group distribution are best shown in duodenal-ulcer subjects who are non-secretors.

Department of Medicine,
University of Sydney, N.S.W. B. P. BILLINGTON.

PARADOXICAL ELECTROCARDIOGRAM IN CORONARY EXERCISE TEST

SIR,—Dr. Geoffrey Bourne [18] states that he has been unable to find any previous report of the "paradoxical . . . result of an exercise test". Dr. Bourne will find a number of examples published in the papers of Alzamora-Castro. I have observed this phenomenon rather frequently when ischæmia is responsible for small inverted or diphasic T waves.

Actually, in addition to the speculations quoted by Dr. Bourne there are two different ways in which the T wave may be paradoxically reversed by exercise—by the occurrence of an injury shift of opposite direction to that of the T wave, and as a result of increase in the rate of repolarisation in ischæmic muscle due to increase in rate. A third and spurious mechanism must be considered. Even if the electrodes are fastened to the chest, the altered position of the heart, due to respiratory phenomena associated with exercise, changes the position of the electrodes in relation to the heart. This may be evidenced by changes in the QRS complexes such as are seen in Dr. Bourne's records. At times, however, the QRS change is not sufficiently great to be evident. Dr. Bourne (or anyone) may strap the electrodes to the chest of his patient with diphasic T waves and study the effects of a deep breath and of forced expiration.

New Orleans. MANUEL GARDBERG.

SIR,—We have read with much interest Dr. Bourne's article.[18] We have often observed the phenomenon he describes in the cardiological clinic of the Greek Red Cross Hospital (director, Dr. C. Maroulis) in the past two years, but have not published our observations. It is very important to know its prognostic significance, compared with that of the ordinary electrocardiographic

12. Clarke, C. A., Edwards, J. W., Haddock, D. R. W., Howel-Evans, A. W., McConnell, R. B., Sheppard, P. M. *Brit. med. J.* 1956, ii, 725.
13. Billington, B. P. *Aust. Ann. Med.* 1956, **5**, 141.
14. Balme, R. H., Jennings, D. *Lancet*, 1957, i, 1219.
15. Hartmann, G. Group Antigens in Human Organs. Copenhagen, 1941.
16. Clarke, C. A., McConnell, R. B., Sheppard, P. M. *Brit. med. J.* 1957, i, 758.
17. McConnell, R. B., Sheppard, P. M. *Acta genet. statist. med.* 1957, **6**, 574.
18. Bourne, G. *Lancet*, 1957, ii, 1320.

response after exercise, and we should very much like to know Dr. Bourne's views on this point.

Greek Red Cross Hospital, Athens. MICHAEL MILINGOS.

ANTIBIOTIC PROPHYLAXIS

SIR,—May I correct Dr. Jhaveri's misapprehension (Feb. 1) of the point of my previous letter (Jan. 18). The point was not that antibiotics are more toxic than sulphonamides but that their use may cause a state of allergy with the direst consequences if the same antibiotic has to be used later to cure an infection. I have never found that sulphonamides, in the doses used as a cover for dental extractions, are toxic or provoke allergy.

Secondly, I should explain to Dr. Sklar (Feb. 1) that I do not use sulphonamides for the treatment of arthritis accompanied by focal sepsis, but solely as a prophylactic measure for a short period before and after an operation dealing with the focus. As I said in my letter, I used to prescribe sulphathiazole 1 g. 4-hourly for 24 hours before and 48 hours after the operation. Recently, however, I have used sulphamethoxypyridazine ('Lederkyn'). With this long-acting sulphonamide I have found that 1 g. daily, for the same length of time, provides adequate cover.

In the 1930s Okell and Elliott [1] found on blood-culture very definite bacteriæmia after tooth extraction, and Fischer and Gottdenker [2] found the same after tonsillectomy. Before that I had seen three patients with early arthritis who became completely crippled after the extraction of infected teeth. The question now at issue is: what is the best drug to render the blood sterile after the influx of potentially infective bacteria? Since sulphonamides are at any rate successful in preventing exacerbation of the arthritis, and by inference rendering the blood sterile, there is no justification for prescribing antibiotics.

My thanks are due to Messrs. Lederle for a supply of 'Lederkyn'.

London, W.1. H. WARREN CROWE.

CARDIAC ARREST FOLLOWING ELECTROPLEXY

SIR,—This brief account may be of interest, particularly to psychiatrists.

A man who had previously had much electroconvulsive therapy had a further treatment in a hospital outpatient department. After an injection of atropine 45 minutes before, thiopentone (0·2 g.) and suxethonium bromide (100 mg.) were given intravenously. Having had a convulsion, the patient began to breathe normally; and oxygen was given at first. At this stage he was not cyanosed and his pulse was normal.

About 5 min. later, breathing ceased and the pulse disappeared. He was extremely pale and appeared to be dead. Auscultation showed that the heart had stopped. Nikethamide (2 ml.) was immediately given intravenously, and artificial respiration with oxygen given, but without any immediate effect. Cardiac arrest lasted at least 3 minutes and probably more. There was a sudden convulsive gasp, and as the stethoscope was applied the first beat of the heart was heard, followed after an interval by infrequent irregular beats and then a fast regular rhythm.

Respiration was complicated by laryngeal spasm and stridor, resembling croup in a child. This was replaced after about 10 min. by severe bronchospasm. Atropine and then adrenaline were given. The patient was unconscious during all this time. Eventually he recovered fully and was none the worse for his experience.

The significance of this incident lies in its bearing on the occasional mortality associated with electroplexy. This treatment is very effective in many cases, but there is still uncertainty about contraindications. The use of muscle relaxants has obviated the risk of fractures and excessive exertion in the elderly, but the unpleasant subjective feelings necessitate the use of short-acting barbiturates. Both types of drug have been blamed for adding a further risk to a relatively safe treatment.

In this case it seems that parasympathetic excitation led first to vagal inhibition of the heart, then to laryngeal spasm, and later to bronchospasm.

This case indicates that the dangers of electroplexy may lie not so much in the actual fit, but in the aftermath, when parasympathetic overactivity may inhibit the heart. The immediate treatment should be atropine or a similar drug, and it is wise to give it always before treatment.

Saxondale Hospital, Radcliffe-on-Trent, Notts. P. J. CROWLEY.

1. Okell, C. C., Elliott, S. D. *Lancet*, 1935, ii, 869.
2. Fischer, J., Gottdenker, F. *Wien klin. Wschr.* 1936, **49**, 177.

PHOTOGENIC EPILEPSY

SIR,—I was interested to read the paper by Dr. Hutchinson and his colleagues (Feb. 1). Recently I saw a patient whose attacks of major epilepsy appeared to be induced by photic stimuli in a rather unusual manner.

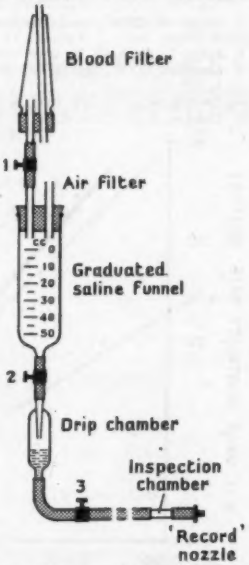
The patient was a man of 27 who was an electrician employed by a television-hire company. On two occasions he was called to customers' homes to deal with what proved to be an identical fault as a result of which the screen emitted a rapidly flickering light. After a few minutes' exposure he lost consciousness on both occasions. He gave no previous or family history of epilepsy, and a year had elapsed between the attacks.

Electroencephalographic examination revealed a normal resting record, but during photic stimulation there were a number of brief generalised outbursts of slow activity and spikes suggestive of idiopathic epilepsy.

Dryburn Hospital, Durham. G. ISMAY.

A BURETTE FOR GIVING INFUSIONS TO INFANTS

SIR,—One of the difficulties that beset those who give intravenous fluids to infants is that of regulating the flow-rate of the infusion accurately. In a report on variation in the rate of flow of drip infusions Dr. J. N. Walton described a piece of apparatus which obviates this difficulty.[1] Using similar apparatus at the Royal Waterloo Hospital, we have found that it combines the advantages of simplicity and ease of sterilisation.



A standard transfusion set is used, with extra long tubing to facilitate the changing and feeding of the infant. A burette is incorporated between the blood filter and the drip chamber. It consists of a graduated saline funnel (as used for tube-feeding infants) with a two-holed rubber stopper containing two short lengths of glass tubing, one of which acts as an air inlet and contains a plug of cotton-wool as an air filter. A gate clamp above and below the burette serve to refill it with fluid each time it becomes empty. Another gate clamp below the drip chamber regulates the flow-rate of the drip.

1. Walton, J. N. *Lancet*, 1947, i, 662.

The infusion is set up in the usual way, the burette being filled by opening gate clamp (1). Air is then expelled from the system by opening gate clamp (2) to allow the fluid to flow through the tubing. When the infusion has been set up and regulated, the gate clamp (3) need not be touched except to readjust the rate of flow of the drip if necessary.

Detailed instructions can be given to the nurses as to how often the burette is to be replenished, and hour-to-hour control over the rate of flow of the drip becomes possible.

My thanks are due to Dr. B. D. R. Wilson for his help, and also to Messrs. Allen & Hanburys, from whom the apparatus may be obtained. 50 ml. graduated saline funnels with two-holed rubber stoppers are made by H. W. Bush & Co. of Croydon and are stocked under the number 364 G.

St. Thomas's Hospital, London, S.E.1. P. C. BEWES.

TREATMENT OF BREAST CANCER

SIR,—In your leading article of Feb. 1, and in Professor Smithers's masterly summing-up last week, the Birmingham figures are mentioned. At least two of these figures need explanation.

On p. 9 of the report,[1] in table 4, survival-rates are quoted where carcinoma of the breast is complicated by pregnancy. Here it is stated that where pregnancy occurred after treatment the three-year survival-rate was 73·3% and the five-year survival-rate was 75%. Does this, perhaps, include the child?

Bangor. W. SKYRME REES.

PREMEDICATION FOR GASTROSCOPY

SIR,—Gastroscopic examination is usually carried out under local analgesia, though Goligher and Thornton [2] advocate general anæsthesia, which has a useful place in selected cases.

The local agent is a cocaine derivative, and one of the least toxic and most reliable is lignocaine, used in the lozenge form in a dose of 250 mg. Anæsthesia is adequate if the tablet is allowed to dissolve in the mouth and the resultant suspension gradually swallowed. Viscous lignocaine can also be used, but the injection technique is now rarely used.

To prepare the patient for this examination, sedation is necessary and some form of opiate is normally prescribed. This is unsuitable for outpatients and has several other disadvantages. The commonest combination is morphine sulphate gr. $^1/_4$ and atropine sulphate gr. $^1/_{100}$, but, in my experience, nausea may occur with considerable "gagging".

In a series of 100 consecutive elective admissions to hospital, the patients were given morphine gr. $^1/_4$ as a test. 7 vomited and a further 10 felt miserable with nausea.

The incidence of such symptoms, using morphine and atropine, was 14% in a series of 250 endoscopies. In these, the examination was not only unpleasant to the patient but also difficult for the examiner. As various opiates seemed to behave similarly, it was decided to try an alternative.

A drug is needed to relieve anxiety without loss of cooperation, to sedate without drugging, to allay nausea and retching, and to enhance analgesia. Chlorpromazine hydrochloride, highly successful in producing tranquillity of mind, and its anti-emetic effect in various disorders, seemed worth a trial.

It was given intramuscularly, in a dose of 50 mg., with atropine sulphate gr. $^1/_{100}$, thirty to forty-five minutes before the anæsthetic lozenge, and the effect has been very satisfactory. In 200 consecutive examinations, only 5 patients had any significant gagging and feeling of sickness, and all others felt relaxed and unperturbed by the procedure. While the number of cases is perhaps small for statistical accuracy, the improvement in the comfort of the patient has been striking. No complications have been seen, and the technique seems satisfactory for outpatients. Toxic effects after a single dose are extremely unlikely and have not been observed.

Chlorpromazine hydrochloride is therefore recommended as a safe and reliable premedication for gastroscopy.

Glasgow Royal Infirmary. DAVID C. MILN.

ÆTIOLOGY OF PRE-ECLAMPTIC TOXÆMIA AND ECLAMPSIA

SIR,—Professor Browne is to be congratulated on his comprehensive paper of Jan. 18. He states, "we now have all the essential facts bearing on the ætiology of eclampsia". I would venture to disagree with this, because he fails to give a satisfactory explanation of the cause of the basic pathological feature of pre-eclampsia—namely, placental ischæmia.

Professor Browne attempts to explain the cause of placental ischæmia as being overdistension of the uterus in twin pregnancy, and stretching against powerful resistance in primigravidæ; but toxæmia can arise early in pregnancy before there is any overdistension, or before undue stretching of the uterine muscle has occurred. Moreover, hypoplasia of the vascular system cannot be the explanation, because toxæmia can be severe in "grand" multiparæ. Chronic hypertension, causing diminished placental blood-flow, is also not a satisfactory explanation, for toxæmia can occur in non-hypertensive patients. In addition, Professor Browne has explained hypersensitivity of the vascular system as being due to increased chorionic gonadotrophin, but he goes on to admit that this sensitivity of the vascular system, which plays a part in the ætiology of toxæmia, is acquired "from whatever cause in pregnancy". Dornhurst and Young [1] found in guineapigs and rabbits that injections of *l*-adrenaline and *l*-noradrenaline caused a reduction in the maternal placental circulation—a reduction shown by Browne and Veale [2] to exist in cases of pre-eclampsia hypertension in the human. Further, they believe that this reduction is not due to the uterine contractions.

In another part of his discourse Professor Browne discusses the role of diet in causing toxæmia and in the end could offer no better explanation than increased output of corticotrophin—a fact for which, when discussing toxæmia in diabetic pregnancies, he says there is no evidence.

In this department work has been going on for some years in an attempt to identify the pressor factor in the blood of toxæmia patients. Some evidence has been collected that the pressor factor may be noradrenaline.[3] It seems that there has been a concentration of research on the adrenal cortex, overlooking possible trigger-factor in the adrenal medulla.

The outstanding feature of pre-eclampsia is generalised vasoconstriction—particularly in the liver, uterus, placenta, and kidneys. Grayson and Johnson,[4] using rats and rabbits, found that "intravenous or subcutaneous noradrenaline frequently produced a diminution in liver blood flow, the local action overriding the reflex dilator action of the raised blood pressure", and that "the local action of noradrenaline on the liver vessels was constrictor". Inadequate intake of protein may lead to diminution in the amount of methionine from the liver necessary to methylate noradrenaline to adrenaline. Hence, the original fault may be inadequate protein, a factor which would be present throughout pregnancy, and indeed it

1. The United Birmingham Hospitals Annual Cancer Report, 1957, vol. 3, Breast.
2. Goligher, J. C., Thornton, H. L. *Lancet*, 1951, ii, 652.

1. Dornhurst, A. C., Young, I. M. *J. Physiol.* 1952, **118**, 282.
2. Brown, J. C. McC., Veale, N. *J. Obstet. Gynæc., Brit. Emp.* 1953, **60**, 142.
3. Lennon, G. G., Gardiner, J. *ibid.* (in the press).
4. Grayson, J., Johnson, D. H. *J. Physiol.* 1953, **120**, 73.

would seem that pre-eclampsia is a disease very often built up over a considerable time in pregnancy, and very often controlled by high-protein diet, especially in its early stages. Sims [5] states, "the raised excretion of methionine and choline characteristic of the pregnant state is detectable by the end of the first trimester . . . with the methionine there is a falling off in the last trimester probably due to some degree of methionine depletion of the maternal organism at this time."

Noradrenaline can raise both systolic and diastolic blood-pressure and can produce a complete arrest of renal blood-flow. Our evidence that the pressor factor is noradrenaline in the blood of the toxæmic woman has been deduced by chromatogram extraction, by biological assay in rats, and by the neutralising of the pressor factor by dibenylene. I would suggest that increased circulation of noradrenaline in the pregnant toxæmic woman is a sufficient explanation of vascular spasm leading to so many of the pathological findings in pre-eclampsia and eclampsia, and especially to the reduction in placental blood-flow and placental ischæmia.

Professor Browne has stressed the clinical similarity of Cushing's syndrome and pregnancy toxæmia. But I believe that there is a closer clinical similarity in the effects of phæochromocytoma and toxæmia. Gemmell [6] has referred to this.

Other work in this department confirms the rise of blood-pressure in the third stage of labour and afterwards in many normal cases. The peak occurs about half an hour after the birth of the child.[7]

I hope that these remarks do not in any way detract from the most excellent paper of Professor Browne and that they merely help to show that "all the essential facts" bearing on the ætiology of this distressing subject have not yet been elucidated.

Department of Obstetrics and Gynæcology, University of Bristol. G. GORDON LENNON.

TRICHOMONAS VAGINALIS

SIR,—I had hoped for many more comments on this subject, especially concerning those most distressing and difficult cases—the recurrences.

The success of any treatment administered by the patient is prejudiced by a lack of cooperation from a class of patient who expect immediate relief, if not cure.

In treating vaginal discharges, relief from irritation and soreness is so paramount a feature that any treatment which fails in this is often discarded by the patient. A second essential is that the preparation must be æsthetically acceptable to both female and male if necessary. Finally and naturally, the preparation must be effective, and if it has a wide range of activity, such as that claimed for 'Locan' pessaries and cream in the report from Dr. Stewart and his colleagues (Nov. 23), it will be most welcome by clinicians.

My own impression is that, while many preparations fail on one or more of these criteria, locan appears to fulfil all three, and is, therefore, a most valuable addition to our range of local applications.

Croydon. J. C. MILLER.

BEE STINGS

SIR,—Reactions of moderate severity to bee stings are not uncommon even among bee-keepers; I myself have kept bees for the past few years and am nearly always stung when I interfere with my bees. On these occasions I usually experience general malaise and fever up to 100°F which may continue for two or three days, together with local pain, swelling, and itching. I have found in my own case and in three other instances that taking 0·5 mg. diphenylpyraline ('Histryl Spansule', Smith, Kline & French) about half an hour before opening the bee-hives prevents all the unpleasant effects. I have also found that as the season progresses I can do without the drug, suggesting that the normal development of immunity is not prevented. Local application of antihistamine cream after being stung is useless in such cases as my own. Some bee-keepers who have had to abandon their occupation on account of reactions to stings could probably have been helped by the simple therapy described.

Eridge, Sussex. F. J. PRIME.

TREATMENT OF MYXŒDEMA

SIR,—Dr. Gibson (Feb. 8) has not given the information we hoped for—namely, what method and standards he used for determining his patients' B.M.R.s. Terms such as swinging to the right and left are not very helpful unless we are told above and below what limits the B.M.R. is supposed to be swinging.

Dr. Gibson's views are unorthodox, for most clinicians believe that the B.M.R. is of absolute significance in myxœdema—i.e., the advanced stage of hypothyroidism.

Department of Chemical Pathology, West London Hospital, London, W.6. I. J. L. GOLDBERG M. J. SEAMAN.

RECTAL RESERPINE

SIR,—The parenteral administration of reserpine may be needed for the emergency treatment of impending hypertensive encephalopathy or cardiac asthma, and for maintenance therapy in mental illness and in children who find difficulty in swallowing tablets. Occasional difficulties with injections have prompted me to prepare and try suppositories of reserpine in coco butter as an alternative.

Each suppository contains 3 mg. reserpine and weighs 2 g. The suppositories were well tolerated, and no sign of rectal irritation was recorded in 31 adult hypertensive patients in the Alexandria University Hospitals.

The effects of these suppositories were compared with those of 3 mg. reserpine, injected intramuscularly in the same patients. Table I shows the hypotensive response to reserpine by both routes, and the efficacy of reserpine suppositories is apparent. A significant hypotensive effect was recorded in 30 out of 31 patients using these suppositories, while the intramuscular injection produced a significant response (a drop of

TABLE I—FALL IN BLOOD-PRESSURE

	Fall in blood-pressure			
	Systolic		Diastolic	
	Intramuscular	Suppository	Intramuscular	Suppository
Whole series:				
Mean drop (mm. Hg) in:				
1st 6 hours	20	32	12	17
1st 12 hours	21	28	13	16
24 hours	20	26	13	14
Maximum mean drop (mm. Hg)	26	40	15	21
In a single case:				
Maximum drop (% of original pressure)	28	38	32	35
Maximum drop (mm. Hg)	65	80	45	45
Maximum mean drop* (mm. Hg) in-				
1st 12 hours	48	55	26	27
24 hours	42	44	25	25

* The mean of the pressure falls recorded in the first 12 hours and in 24 hours was calculated in each case. The largest mean in the whole series is the maximum mean drop.

5. Sims, F. H. *J. Obstet. Gynæc., Brit. Emp.* 1951, **58**, 985.
6. Gemmell, A. *ibid.* 1955, **62**, 195.
7. Edwards, E. M. *ibid.* (in the press).

at least 20 mm. in systolic pressure and 15 mm. in diastolic pressure) in 29 cases.

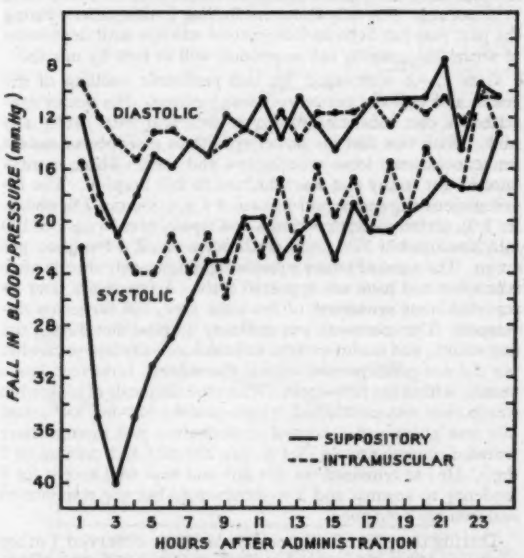
Table II shows that during the first six hours of administration, the number of patients who responded when suppositories were used was almost twice the number responding when the intramuscular route was used. The figure represents the

TABLE II—NUMBER OF PATIENTS RESPONDING TO 3 MG. OF RESERPINE

Time after administration (hr.)	Fall in systolic pressure		Fall in diastolic pressure	
	Intramuscular	Suppository	Intramuscular	Suppository
1 hr.	9	17	4	9
2 „	16	25	10	24
3 „	17	28	12	25
4 „	21	23	13	20
5 „	16	20	12	16
6 „	11	20	9	17
7 „	18	18	16	12
8 „	15	15	12	15
9 „	16	17	15	9
10 „	16	15	12	12
11 „	18	17	16	12
12 „	12	19	11	17

average drop of the blood-pressure in the whole series after the administration of 3 mg. by each route.

Thus, reserpine suppositories have a rapid, sustained and significant hypotensive effect when compared with the intramuscular injections. The rapid action is explained by the rich vascular drainage of the rectum; the sustained action is due to the bigger mass of fat in the rectum from which the drug diffuses much more slowly than from



Average fall in blood-pressure in whole series after reserpine 3 mg.

muscle tissues. Sheppard et al.[1] showed that radioactive reserpine disappeared from the organs and the tissues in two hours, while, in contrast, fat tissues still contained a high amount of radioactive material up to six hours later.

The bradycardic effect of reserpine, administered rectally or intramuscularly, was more or less the same. The suppository dose of reserpine is equal to the parenteral dose.

Faculty of Medicine,
Alexandria University, Egypt. M. H. GHANEM.

1. Sheppard, H., Lucas, R. C., Tsien, W. H. *Arch. int. Pharmacodyn.* 1955, 103, 256.

SYRINGES: CLEAN OR STERILE?

SIR,—I was a little disturbed to see Dr. Jackson's reference (Feb. 1) to sterilising his syringes in a hot-air oven at 160°C.

When testing a large variety of ovens, we found that some were extremely variable when loaded, and this does not seem to be generally appreciated.

As an example, an oven which was within ±3°C when empty with the thermometer registering 160°C, gave temperatures varying between 140°C and 188°C, with the thermometer registering 160°C, when three-quarters full with well-spaced syringes in baskets.

This means that a fair proportion of these would certainly not have been sterilised, since I believe that the latest work by Dr. Darmady shows that a minimum of 160°C is necessary for certain spores.

Perhaps Dr. Jackson would care to insert a number of thermometers in different places and try to check that he runs the coolest part of his oven right up to temperature, bearing in mind particularly that what is wanted is the temperature inside the barrel of the syringe and not in the air of the oven.

Townson & Mercer Ltd., Croydon. R. BARRINGTON BROCK Director.

ATARALGESIA

SIR,—I am grateful to Dr. Selwyn Crawford (Dec. 14) for raising some points which I did not make clear in my preliminary report (Nov. 16).

My primary object has been to devise a method which, especially in disasters and war, will relieve pain, preserve the cooperation of the injured, increase the proportion of "walking wounded", and reduce the quantities of anæsthetics and post-operative medication required. The following additional reports of the use of my pethidine-amiphenazole-'Pacatal' (and/or chlorpromazine) combination illustrate some of the possibilities:

CASE 1.—A policeman was given 3 units by intramuscular injection in the ward, after which, in the theatre, both big-toenails were avulsed and the nailbeds scraped. He carried on an animated conversation the while, screwing up his face, but making no attempt to withdraw his legs as each nail was removed. He then stepped unaided off the table, and walked five yards to the trolley. The sensation, he said, was similar to that of stubbing his toe "but not nearly so bad".

CASE 2.—A man of 28 had extensive (25%) acid burns of legs, thighs, genitalia, and lower abdomen. He was given 3 units and a full toilet was performed. Subsequent dressings were intolerable except under 2 units. (A placebo injection did not mislead him.)

CASE 3.—An Indian woman of 42 received 2½ units intramuscularly after which her fractured radius and ulnar bones were reduced while she stood. She walked to the X-ray department and returned with her wet films; the position being unsatisfactory, the fracture was manipulated several times more, after which she again acted as her own messenger to and from the X-ray department. She seemed "amused about the whole affair".

CASE 4.—After 1½ units, a boy of 7 climbed out of bed, walked to the theatre, mounted the table, and opened his mouth, from which eleven teeth were extracted. He looked like whimpering once, but was distracted. Sliding off the table, he announced that three of the pennies presented to him would be spent on sweets, and the remaining eight would be saved up.

While working up to the present combination, I conducted 29 surgical cases using pethidine-amiphenazole-chlorpromazine (and/or promethazine) in increasing doses. As in Dr. Crawford's obstetric cases given pethidine and chlorpromazine, these patients showed "disturbance of mind" (semi-drunken—probably because they had chlorpromazine instead of pacatal) and thus did not attain true ataralgesia, although 12 required no complementary anæsthetic. It was to emphasise the retention of mental clarity under the pacatal mixture that I administered 2 units to myself half an hour before reading my paper to the South African Medical Congress last September.

The patients for cæsarean sections were given 2½ units intramuscularly in the ward one hour preoperatively (no other

premedication). The infants were born 79, 105, and 82 minutes later respectively. All babies have cried immediately and lustily. Relaxation was adequate but not perfect; and bleeding was minimal.

It is quite possible that levorphanol will prove as satisfactory as amiphenazole. A series is now being investigated for comparison.

I agree that the intravenous route may be advantageous at times, particularly in midwifery; but the central effect is greater; and, if cortical depression is apparent, the case must be classed as an ataralgesic failure.

Ataralgesia is, by definition, contrary to the type of relaxation produced by muscle relaxants—i.e., flaccidity through loss of tone. When the relaxation required is really an overcoming of spasm due to pain—as with fractures, dislocations, trismus, or thoracic immobilisation—ataralgesia is usually sufficient in itself. It does not, of course, relax abdominal muscles; but factors such as laxity of muscles, or even shock may facilitate abdominal surgery; and in the event of mass casualties much pain-free repair could be undertaken, albeit under less than ideal conditions.

In my paper, no claim was made that intra-abdominal operation (apart from the cæsarean sections) was performed under successful ataralgesia. Nevertheless, five such operations were performed without complementary anæsthesia. A transdiaphragmatic nephrectomy for a stab wound required assisted respiration only. A Wertheim's hysterectomy, an operation for intestinal obstruction, excision of a large chorion epithelioma, and a 210-minute gastrectomy were all performed, increasing the central effect and using intermittent minimal doses of gallamine. Intubation is quite possible without a hypnotic (cf. conditions under the " lytic cocktail ").

I must repeat that my report was a preliminary one and as such left much unsaid. It has been clear from these investigations, however, that there are many sidelines and other applications of ataralgesia, as well as deliberately modified forms of it in surgery, medicine, dental and veterinary work, and, in particular, obstetrics.

Durban, South Africa. J. T. HAYWARD-BUTT.

SIR,—Under the guidance of Dr. Hayward-Butt, I have been using " ataralgesia " in obstetrics. The following interim report of ten normal deliveries may be of interest.

A combination of pethidine, amiphenazole, and ' Pacatal ', using $2^1/_2$ units, was given when the patient's cervix was approximately four-fifths dilated. The average period between its administration and the delivery of infant was 55 minutes. In no case was the newborn infant distressed. The average period between the infant's birth and its first cry was $1^1/_2$ minutes. All mothers reported marked relief of pain and only one was uncooperative after the injection. Intravaginal manipulations caused no pain or complaint. There were no cases of postpartum hæmorrhage and, apart from acute mastitis in one case, no postpartum complications.

Two forceps deliveries were also performed with satisfactory results:

CASE 1.—Mrs. A., aged 17, 42 weeks pregnant, went into labour at 9 A.M. At 1 P.M. the cervix was fully effaced and dilated, the vertex presenting in transverse diameter. After $^3/_4$ hour, no advance was noted and pethidine-amiphenazole-pacatal ($2^1/_2$ units) was given by intramuscular injection. 12 minutes later, forceps was applied and a live female infant weighing 8 lb. was extracted. The placenta was expressed 5 minutes later; there was no abnormal blood-loss. The application of forceps was easy; the patient experienced no pain and was cooperative at all times.

Before extraction of the head, episiotomy was undertaken and, as the patient felt some pain, 1% lignocaine was given in the line of the incision.

CASE 2.—Mrs. B., aged 38, 4-gravida, went into labour at 10 P.M. Vaginal examination at 8 A.M. next day showed the cervix to be fully dilated with the vertex presenting in transverse diameter. As the patient was distressed, forceps delivery was decided on and pethidine-amiphenazole-pacatal was given at 8 A.M. At 8.30 A.M. a live male infant was extracted with forceps. He cried immediately; the placenta was expressed after 7 minutes, and there was no postpartum hæmorrhage.

Manual removal of the placenta was performed in another patient. She was cooperative and felt no pain.

The results in this small series suggest that, when given with amiphenazole, large doses of pethidine (up to 300 mg. half an hour before delivery of the infant) could safely be used in obstetrics.

Durban, South Africa. C. J. GOOSEN.

IDIOPATHIC STEATORRHŒA WITH HYPOPROTEINÆMIA

SIR,—Dr. Forshaw has reported a case of idiopathic steatorrhœa with severe hypoproteinæmia [1]. We should like to report 2 similar cases and make some comments on the subject.

CASE 1.—A man, aged 56, had noticed swelling of the ankles and legs for three weeks. The swelling had varied somewhat and tended to increase after heavy work. He had been given digitalis, but as this drug had no effect on the swelling he was sent to hospital. He had moderate œdema of the ankles and legs. The serum-protein was 4·4 g. (albumin 1·5, globulin 2·9), serum-calcium 7·6 mg., and serum-iron 62 μg. per 100 ml., hæmoglobin 73%, and erythrocyte-count 3·8 million per c.mm. He was first treated with a high-protein diet for six weeks, without appreciable effect on the serum-protein. When the diagnosis was established he also got a low-fat, low-cereal diet, and in another six weeks the serum-protein increased from 4·8 to 6·5 g. per 100 ml. and the œdema disappeared. He has since had the same diet, and serum-protein and calcium values have been normal. The only abnormal finding in this patient during the past year has been an intermittent anæmia with depression of serum-iron, which has responded well to iron by mouth.

CASE 2.—A man, aged 39, had persistent swelling of the ankles and legs and periods of loose motions. His doctor prescribed a diet consisting mostly of fish, and with hardly any milk. With this diet his bowel symptoms disappeared except for an occasional loose motion now and then. Three months later he got tetany and was admitted to this hospital. The investigations showed serum-protein 4·9 g. (albumin 2·0, globulin 2·9), serum-calcium 6·1 mg., and serum-iron 26 μg. per 100 ml., hæmoglobin 77%, and erythrocyte-count 4·1 million per c.mm. The signs of tetany subsided spontaneously shortly after admission and have not appeared since. A few weeks later he reported some sensations of the same type, but no tetany developed. The treatment was ordinary hospital diet during the first month, and serum-protein and calcium increased somewhat but did not reach normal values; the œdema, however, disappeared, within the first weeks. When the diagnosis of idiopathic steathorrœa was established, a high-protein, low-fat, low-cereal diet was given and a control investigation two months later revealed normal protein (7·4 g. per 100 ml.) and calcium (9·7 mg.). He has remained on this diet and kept well except for a tendency to anæmia and low serum-iron, but the response to oral iron has been good.

During the past fifteen months we have observed 2 other patients with idiopathic steatorrhœa.

CASE 3.—A man, aged 65, had for many years had intermittent bowel symptoms. His symptoms increased, with anorexia and loss of weight. He had no œdema, but the serum-protein was 5·0 g. per 100 ml. He is keeping well on the diet described above and the serum-protein has become normal.

CASE 4.—A man, aged 52, had for some months had anorexia, loss of weight, and bowel symptoms. A year previously he had had the same symptoms for some weeks, but recovered spontaneously. He was very ill on admission with a serum-protein of 4·1 g. per 100 ml. Despite all therapy he died six weeks later.

We are not convinced that hypoproteinæmia is as unusual in idiopathic steatorrhœa as Dr. Forshaw states.

1. Forshaw, J. W. B. *Lancet*, 1957, ii, 720.

The protein metabolism in this disease has not attracted much attention until recent years, and we believe there is increasing evidence that the albumin, at least, is often decreased to some extent. Adlersberg et al. [2] report serum-protein determinations in 67 patients with idiopathic steatorrhœa, and in 19% of these the total protein content was less than 5 g. per 100 ml. In 60 of these patients the serum-albumin was determined; in 52% it was less than 3·5 g. per 100 ml. In 16 patients (24%) œdema was present at the time of admission.

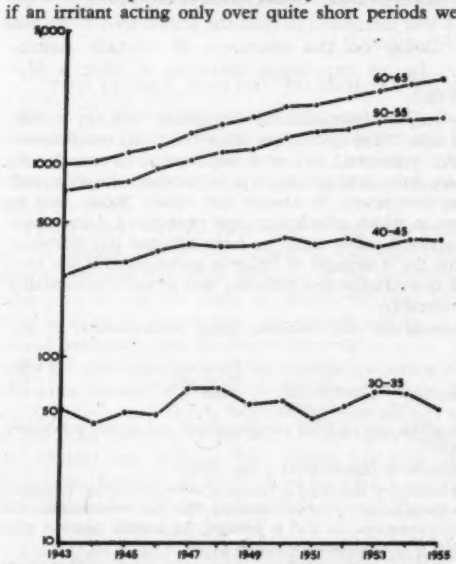
Medical Department, County Hospital, Falköping, Sweden. HOLGER WAHLUND
NILS D. WESTAD.

ANOTHER CANCER FALLACY

SIR,—Your lucid annotation on the fallacy of the decreasing lung-cancer death-rate with extreme age appears to condone the almost identical fallacy of the latent period of the effects of the cigarette. It states that " those now 65 have been more exposed to this hazard ". It might be preferable to state that they "are being more exposed ".

Although analogies from mice and mule-spinners, and the assumptions implicit in the remarkable strategy of contemporary experimental research, may lead to an expectation of a latency of several decades, the available data on man do not allow the inference that the memory of the lung for tobacco is more than a few years.

The apparent latent period between the imports of tobacco and the consequent deaths is exactly what would be expected if an irritant acting only over quite short periods were to be



Deaths from lung cancer in males in England and Wales in 1943-55.

the daily indulgence of a population whose resistance to neoplasia was steadily reduced with advancing age, and whose smoking habits were largely determined in youth.

This fallacy is of some importance not only in relation to the relevance of research on animals not liable to spontaneous bronchial neoplasms, but also in that many middle-aged smokers, fearing that their lungs will always carry the scars and memories of past decades, see no reason to protect their bronchi from further irritation.

As the liability to death from lung cancer doubles every 3 to 4 years between the ages of 30 and 70, the basic rate being 10–20 times higher in the heavy smoker than in the non-smoker,[1] the present virtual restriction of preventive measures to schoolchildren cannot be expected to have much influence on the death-rate until almost a million persons have died from this disease in Great Britain alone. Some idea of the appalling risks to which the ageing smoker is increasingly exposed may be conveyed from the calculation that a free issue of cigarettes to old-age pensioners would save the Government the greater part of the cost of the tobacco.

The accompanying figure gives some idea of the present pattern of increase in this disease.

Department of Social Medicine, Medical School, Birmingham. J. H. EDWARDS.

INFLUENZAL ENCEPHALITIS

SIR,—The letter of Dr. McGill and Dr. Goodbody last week, recording cases of acute hæmorrhagic leuco-encephalitis and referring to those reported by Dr. Dubowitz (Jan. 18), prompts us to make it known that three fatal cases of leucoencephalitis have come to necropsy in this area during the past few weeks. The naked-eye appearances of the brain were closely similar to those depicted by McGill and Goodbody.

In addition we are aware of other cases in which the patients have apparently recovered completely, and at least one other where the issue is still in doubt. We have not observed a clear association in these cases with an immediately preceding attack of influenza. Nevertheless in view of the foregoing reports we think it desirable to publicise the fact that cases of hæmorrhagic leuco-encephalitis are occurring in widely separated parts of the country.

It is hoped that every opportunity will be taken by all who observe such cases to search for an infecting virus both during life and at necropsy.

Pathology Department, University of Glasgow. JOHN H. STEPHENS
D. F. CAPPELL.

INFORMAL ADMISSION OF MENTAL DEFECTIVES

SIR,—I have read with interest Dr. Heaton-Ward's letter (Feb. 8).

While Memorandum H.M.(58)5 recommends the informal admission of suitable cases to mental-deficiency hospitals and the review of the patients already detained, it does not repeal the present Mental Deficiency Acts.

With regard to the review of patients already in hospital, the medical superintendent is asked to submit to the Board of Control the names of patients who might suitably remain on an informal basis without certification and legal detention.

It appears, therefore, that we can go ahead and take action to implement the recommendations of the recent Royal Commission as far as these concern bringing mental-deficiency hospitals more into line with ordinary hospitals, and use certification and detention only where absolutely necessary for the protection of the patient or the community.

In the case of the majority of our patients the decision will be relatively easy, but there is bound to be a hard core of patients where one would hesitate to dispense with legal control. These cases present great difficulty in any case, but personally I cannot agree that the memorandum will make our task harder. Indeed I regard this circular as being the most encouraging document the mental-deficiency service has received since the report of the first Royal Commission of 1908.

Bromham Hospital, nr. Bedford. T. A. DANBY
Medical Superintendent.

2. Adlersberg, D., Wang, C. I., Bossak, E. T., *in* Adlersberg, D.: The Malabsorption Syndrome; p. 32. New York, 1957.

1. Edwards, J. H. *Brit. J. prev. soc. Med.* 1957, **11**, 10.

NYLON-DARN REPAIRS OF HERNIÆ

SIR,—Mr. Moloney in his excellent paper of Feb. 8 implies inadvertently that the recurrence-rate of 14·3% for simple herniotomy (1940–45) in adult males which I recorded [1] referred to an operation which also included a repair of the fascia transversalis at the internal ring. This was not so. Later in the same article I reported a small series of 9 adult cases in all of whom success was achieved by excision of the sac combined with suture of the ring. This was first done by Marcy of Boston (1871) and since 1951 I have continued to use it successfully in those patients who at operation are found to have entirely congenital sacs with narrow necks.

London, W.1. CAMERON MACLEOD.

SIR,—I was much interested in Mr. Moloney's article. The results are excellent by any standard, and must be a strong argument in favour of nylon as the most useful suture material. May I add one criticism and one comment.

The results appear to have been ascertained by a postal questionnaire. Many patients are unaware of a recurrence (or even of a primary hernia) until it strangulates. Furthermore, only 76% of the patients replied to the questionnaire, and there is no reference to the seeking of information from the general practitioners of the missing 24%. The figures for the recurrence-rate cannot, therefore, be anything but very approximate, and cannot be compared satisfactorily with the results of reviews obtained by actual examinations of the patients. Is there no hope of obtaining the results of examinations of these patients?

In the teaching hospitals of the Liverpool region all inguinal-hernia repairs in adult males are registered, and reviewed after one and three years. Between 1951 and 1954, in 450 patients whose hernias were repaired with nylon, 17 developed a sinus failing to heal within two months, 19 further operations were effected to remove pieces of nylon, and 9 cases had a discharge for a year or more—1 for five years. I have not the figures available (as I write) to determine whether the nylon in the affected cases had been monofilament or braided, but I will check this; I think monofilament nylon was used in most of the cases. Admittedly, the cases I quote were dealt with in the main by registrars, whose results one would not expect to equal the personal series of an experienced surgeon. Nevertheless, it cannot yet be accepted that nylon is free from serious disadvantages as a suture material in the repair of inguinal herniæ.

St. Helens, Lancs. A. J. MARSDEN.

TECHNIQUE OF INTRA-ARTICULAR INJECTION

SIR,—Mr. Grant Waugh's letter of Dec. 28 is indeed timely. Much relief can be given to patients by the use of intra-articular injections of hydrocortone, but there is no need for this to be associated with any pain or discomfort.

The knee-joint is treated most frequently and I feel that more consideration should be paid to the injection route in an attempt to avoid pain during the procedure. The usual techniques of injecting on either side of the patellar tendon are to be avoided because the needle does not necessarily enter the joint space or even pierce the synovial membrane as the whole of the apparent space between the femoral and tibial condyles is, in fact, occupied by the alar fat pad and if the hydrocortone is deposited in this structure it causes severe pain.

The method adopted in our practice is to displace the patella laterally with the knee fully extended and insert a short small-bore needle into the tense capsule at the "superolateral corner" of the patella. This manœuvre creates an artificial space which is reached by piercing merely skin, subcutaneous tissue, capsule, and synovial membrane without having to traverse any other tissues. This procedure is completely painless and does not require the use of a local anæsthetic. It is also of great value in aspirating the knee-joint.

Durban, South Africa. CYRIL KAPLAN.

ASSISTED RESPIRATION DURING GALLAMINE ANÆSTHESIA

SIR,—In a number of patients who receive gallamine ('Flaxedil') in the course of anæsthesia induction, the initial period of apnœa is followed by tracheal tug. This may persist for a varying length of time while spontaneous respiration is becoming established again.

During the initial phase of tracheal tug, respiration is so depressed that there is little or no movement of the rebreathing bag, to guide the anæsthetist in the timing of assisted respiration.

However, if a finger of one hand is placed over the patient's larynx whilst the other hand grasps the rebreathing bag it is now possible to synchronise assisted respiration with the early efforts of the patient—i.e., with the tracheal tug.

Later, as respiratory efforts increase, it will be found that this method will give better timing of assisted respiration than judgment based upon the fluctuations of the rebreathing bag alone, since the anæsthetist's own reaction time will be shortened.

St. Giles' Hospital, London, S.E.5. P. A. P. POMPA.

INFANTILE GASTROENTERITIS

SIR,—I was interested to read the article by Dr. Brown and Dr. Bailey on the treatment of infantile gastroenteritis.[1] In my experience cortisone is often a life-saving drug.

In the tropics gastroenteritis is usually seen in a very advanced stage. The infants are often practically moribund—dehydrated, cyanosed, and with dry staring eyes. It has always been difficult to get this type of patient, with a sluggish peripheral circulation, to absorb and retain fluids, and in those cases in which rehydration was established dehydration rapidly recurred. But since we have adopted the following routine for the treatment of infantile gastroenteritis we have been able to overcome this difficulty and reduce the mortality very considerably.

(1) Intramuscular drip infusion, using hyaluronidase, of this solution:

Sodium	25 mEq.	Lactate	23 mEq.
Potassium	20 mEq.	Phosphate	3 mEq.
Magnesium	3 mEq.	Water	1 litre
Chloride	22 mEq.		

200 ml. is given into each leg simultaneously and repeated 4-hourly if necessary.

(2) Cortisone intramuscularly 5 mg. 4-hourly.

(3) Antibiotics: if the child is vomiting severely, 50 mg. oxytetracycline is given 8-hourly intramuscularly; but the usual routine has been to give streptomycin 0·25 g. 6-hourly by mouth, together with half a tablet of phthalylsulphathiazole.

(4) Water by mouth, until vomiting stops, then half-strength milk feeds.

Cortisone seems to assist in the rehydration of patients with peripheral vascular failure, and prevents fluid loss once rehydration has been established. It is possible to withdraw the cortisone suddenly about the fourth day, once the diarrhœa has stopped, without ill effects.

Unfortunately it has not been possible to establish scientific figures because staff is short and the pathological department is already overworked. I would add that there is tremendous overcrowding in the wards; isolation is impossible, and very often two infants have to be nursed in the cot. Cross-infection is practically

1. *Lancet*, 1955, ii, 106.

1. Brown, E. H., Bailey, E. H. *Lancet*, 1957, ii, 1218.

never seen and no precautions are taken regarding disposal of napkins or feeding, since there is a great shortage of nurses. I feel, however, that cortisone should be given an adequate trial in a gastrointestinal unit.

General Hospital,
Taiping, Perak, Malaya. B. E. BARSBY.

AMAUROSIS FUGAX

SIR,—Sir Philip Livingston's very interesting article [1] brings to mind a striking case.

A woman, aged about 50, had a large painful ulcer on the right side of her neck, following X-ray and radium treatment for a supposedly malignant tumour. The ulcer was larger than a man's palm, with a hard sloughing base. Its upper edge was 1–2 cm. below the mandible. Biopsy showed no malignant cells.

I began treatment with injections of her own blood (40 ml., not altered by citrate) under the edges of the ulcer—a treatment which I had found successful in previous cases when healing was slow. After two injections the pain was less. At the third treatment, when about 5 ml. of blood had been injected under the superior edge, she suddenly became blind in the right eye; her right eyeball was protruded, and the pupil dilated and insensitive to light. The left eye was unchanged. I stopped the injection; sight returned to the right eye, and was normal in 4–5 min.

War-time conditions prevented me from investigating this case further. I have seen no similar event in over fifty years of practice, and I cannot explain it except as a reflex response. Stimulation of the carotid body was unlikely for anatomical reasons.

Budapest. ANDREW MAKAI.

THE LIONEL WHITBY MEMORIAL FUND

SIR,—We should appreciate your assistance in calling attention to a fund being raised by the Master and Fellows of Downing College, Cambridge, in memory of their late Master, Sir Lionel Whitby, regius professor of physic in the University.

The Lionel Whitby Memorial Fund was established at the suggestion of the Downing College Association and an Appeal has been sent out to its members. It is proposed to use the fund to found Whitby Memorial Scholarships in the college, an object which, it is felt, would have met with his warm approval.

As an undergraduate of the college he was a Scholar, and later became successively Honorary Fellow, Professorial Fellow, and finally Master, and the college was one of the chief interests of his life. It has been suggested to the Master and Fellows that among his wide circle of friends in the medical world there may be many, in addition to members of the college, who would like to contribute to this Memorial Fund.

The Master and Fellows would very much welcome such contributions, as the resources of the college are among the most limited of those of the Cambridge colleges. Although the college now spends from its general resources nearly £4000 annually on scholarships and exhibitions, only about £1000 of this is provided from specific endowments. It was the heavy demand thus made on the general endowments of the college, together with a wish to keep alive the memory of Whitby in the minds of future generations of undergraduates, which led the Association to allocate the present fund to the foundation of scholarships bearing his name.

Contributions should be sent to the Bursar, Downing College, Cambridge, and if so desired, may be made by seven-year covenant, forms for which will be supplied on request.

W. K. C. GUTHRIE
GORDON GORDON-TAYLOR
HAROLD BOLDERO
E. C. DODDS
R. W. SCARFF
JOHN KIRK.

1. *Lancet*, 1957, ii, 1129.

Parliament

Children of Broken Marriages

ON some of their most important recommendations the members of the Royal Commission on Marriage and Divorce were divided. Not unnaturally these recommendations led to controversy and discussion among the public. But the group of recommendations urging that the children of broken marriages should be offered more protection and security was readily accepted on all sides, and on Feb. 7 Mr. ARTHUR MOYLE introduced, as a private member, the Matrimonial Proceedings (Children) Bill which will give legislative shape to the Commission's suggestions.

In his opening speech Mr. Moyle said that each year the parents of over 20,000 children were parted in divorce, which meant that 1 child in 20 was deprived of a normal home. That was not the kind of basis on which children could build well for their future lives. One main provision of his Bill was to ensure that no final decree, either in divorce or judicial separation, could be made final until the court was satisfied that as far as practicable satisfactory arrangements had been made for the future of the children. A second important provision was to set up a court welfare service to assist the judge in reaching decisions about the custody of the children.

Mr. DAVID RENTON, joint under-secretary of State for the Home Department, in welcoming the Bill on behalf of the Government, said that the lives and happiness of a considerable number of children were affected by the disputes of their parents and it was right that the courts should pay regard to their welfare. If the Bill became law he was sure that those who administered the law would welcome the new powers and responsibilities which it would give them.

Shrimps, Prawns, and Pickled Onions

On Feb. 10 Mr. FREDERICK WILLEY prayed against the proposed amendment to the Food Hygiene Regulations (S.I. 1957, no. 2157) which, subject to safeguards, would except shrimps, prawns, and pickled onions from the embargo on the processing of food in the homes of outworkers. Most of the debate rightly centred round the shrimps and prawns, for unlike the onions, they are peeled in the workers' homes after and not before they are boiled, and no form of sterilisation, however informal, comes between them and the consumer. Many members were clearly uneasy about their preparation in the home. Time must elapse between preparation and sale, children must be cared for, babies must be changed, and constant supervision by the manufacturer or the local authority is impossible.

Mr. RICHARD THOMPSON, parliamentary secretary to the Ministry of Health, said that, though there was no reason why food could not be prepared in domestic premises in as clean a way as in a food factory, absence of supervision could admittedly permit lower standards than people nowadays expected for the preparation of food. But the present regulations offered some safeguards. They laid down that outworkers' premises must be registered with the local authorities. Outworkers must also observe the ordinary provisions laid down in the food and hygiene regulations to ensure the personal cleanliness of the worker and the protection of the food from contamination. (These standards do not, however, seem too exigent, for in response to questions Mr. Thompson agreed that an "adequate supply of hot water" did not require a water heater, but could be met by water boiled in

a kettle and that " reasonably accessible " could mean a basin in the next room.) It was, he pointed out, difficult to find workers to undertake these particular jobs, and the Minister had accepted that it would not be practicable to change arrangements in these two industries without severe dislocation. But the Minister also accepted the desirability of replacing outworking as soon as possible by methods which would ensure adequate supervision of peeling. There was provision to review the working of the regulations in two years' time. The motion was withdrawn.

QUESTION TIME

New Drugs

Mrs. SLATER asked the Home Secretary what precautions were taken to protect the public from the marketing of new drugs which might be likely to cause harm to the public if used without proper safeguards.—Mr. DAVID RENTON replied: There are special provisions for the control of drugs coming within the scope of the Dangerous Drugs Act or the Therapeutic Substances Act. Before placing new substances on the market manufacturers take every precaution, if necessary by laboratory tests and clinical trials, to ensure that they are not harmful. Where it is found, either before a drug has been marketed, or afterwards, that it may have harmful effects, the Poisons Board are asked to consider whether it should be controlled as a poison.

Mrs. SLATER: Is not the Minister aware that there is vast and growing concern at the amount of drugs which are now being put on the open market and which can thus be bought quite freely? Is he aware that there have been several cases of people who have suffered very badly—some have landed in mental homes and some have even died—as a result of the free sale of these drugs? Is not it time that these drugs were referred to the Poisons Board before being put on the open market?—Mr. RENTON: I am not sure whether the hon. Lady is referring to what are known as new drugs. If she is, then that is a matter which should be put to the Minister of Health. Of course, a great many of the well-known and established substances are perfectly harmless when taken in moderate quantities and can become dangerous only when taken in excess. There would be no point in making such substances into poisons from the technical point of view. In any event, it is for the Poisons Board to use its initiative in this matter.

Suicide and Attempted Suicide

Mr. KENNETH ROBINSON asked the Home Secretary if he would introduce legislation to amend the law relating to suicide and attempted suicide.—Mr. R. A. BUTLER replied: I am not satisfied that any change in the law is desirable. Mr. ROBINSON: Is the Home Secretary aware of the considerable and growing opinion in the medical and legal professions, and among the general public, that the legal view of suicide is more and more at odds with society? Has not the time come to take this matter completely outside the category of criminal offences?—Mr. BUTLER: The present concept of suicide as a crime has its roots in religious belief. Although it is true that there is greater sympathy and understanding for suicides and would-be suicides, there is no evidence in my possession that the alteration of the basic concept would be universally acceptable to public opinion. I do not underestimate the point that the hon. Gentleman has put to me; I am simply trying to assess the present position.

Certification

Dr. D. JOHNSON asked the Minister of Health whether the statement of Dr. W. S. Maclay, a principal medical officer of his department, made in Toronto on Jan. 22 was made with his authority; and how far the conclusion embodied in it was based on facts collated within his department.—Mr. DEREK WALKER-SMITH replied: I understand that this statement was made in the course of a long and comprehensive address to a meeting of Canadian psychiatrists on British mental health services. It was intended only as a humorous reference to some medical certificates which, as evidence of unsound mind, had been rejected by the Board of Control over a number of years. Dr. JOHNSON: Does not the Minister appreciate that Dr. Maclay, in his statement in Toronto, a report of which stated: ". . . . that doctors' reasons for certifying patients as being of unsound mind 'often makes one wonder whether it is the doctor or the patient who should be certified'"

was, in fact, drawing attention in, perhaps, rather colourful fashion to the same problem of improper certification, and will he not ask Dr. Maclay to amplify his statement on his return to this country?—Mr. WALKER-SMITH: I will certainly discuss it with Dr. Maclay, but I do not think it would be very rewarding to pursue seriously with him something that was meant in lighter vein to sugar the pill of the solid and serious argument to which he was addressing himself on this occasion.

Mr. H. H. DODDS: But how can the Minister justify saying that it was said in fun when thousands of people in this country are being certified by one doctor without any special knowledge of mental troubles? When one of his chief representatives goes abroad and makes a statement like that, how can he say he was just having fun? If the Minister is making fun of it, does he not think of the thousands of people who are having to bear this stigma—and their children and grandchildren? Surely, it is not a thing to make fun about.—Mr. WALKER-SMITH: As I am sure the hon. Gentleman knows, it is not an uncommon practice among practised and persuasive speakers to try to introduce a little lighter note into a serious argument, and it has never been held that that convicts them of any improper levity in their approach to a serious subject.

Social Services

In 1938 about 34% of Central Government current expenditure was on social services; in 1956–57 the figure was 37%. Current expenditure by all public authorities on social services was about 10% of the national income in 1938 and 15% in 1956–57.

Windscale Accident and London

Radioactive iodine was detectable in the atmosphere over London after the Windscale accident on Oct. 11, 12 and 13, 1957, but in very much smaller amounts than in the Windscale area. By Oct. 14 the level had fallen below the limits of detection.

Obituary

GWYNNE EVAN OWEN WILLIAMS

M.D., M.S. Lond., F.R.C.S.

As we announced last week Mr. Gwynne Williams, consulting surgeon to University College Hospital, London, died on Feb. 3.

He was born at Luton in 1881 and went to Bedford Grammar School and later to University College, London. He qualified from University College Hospital in 1903. As a student and resident he played rugby for the hospital, and he was treasurer and president of the medical society. In 1905 he took the M.D. Lond., and the following year the M.S. and F.R.C.S. For a time he held a registrarship at the Seamen's Hospital, Greenwich, but in 1910 he was appointed surgical registrar at U.C.H. Four years later he was appointed surgeon and he held this post until he retired in 1946. He was also on the staffs of the Royal Northern Hospital and the Cheyne Hospital for Children.

During the late war he was in charge of the casualty-clearing services of the hospital, and he lived there during all the air-raids. He gave the hospital notable service as chairman of the medical committee and as dean from 1935 to 1943. A. M. H. G., whom he succeeded in the deanship, writes:

My association with Bill, as he was always called at U.C.H., began when we were students. He was slightly my junior, but

we were in residence together and when we both decided to set up in practice, we took rooms together, which we shared for nearly ten years. We were also closely associated at the medical school. It is difficult for a colleague to assess the professional eminence of another colleague in a different branch of medicine, as one sees little of that side of his work. In fact I don't remember ever having seen Bill operate, but I have been told by surgical colleagues how much they respected his opinion on difficult cases. As a teacher he was superb. Conscientious to a degree and tireless, he got the very best out of his students and though he made their path hard, they loved him for it.

He was of a retiring disposition and to a stranger often appeared to be somewhat fierce. He certainly did not suffer fools gladly, and could at times be rude, but beneath this somewhat forbidding exterior he could be kindness itself, and his many friends will never forget the help he gave them.

To Gwynne Williams' work as a surgeon one of his colleagues, who was once one of his students, pays the following tribute:

His surgery was developed in the days before anæsthetics were as safe or as smooth as they are today, when speed mattered, and the apparently effortless way in which he performed a wide variety of surgical operations was remarkable. He practised before specialisation in surgery was common, but had a particular interest in the treatment of fractures. He was a pioneer in introducing to this country the ambulatory treatment of some leg fractures, and was one of the first to use the Smith-Petersen nail in fractures of the femoral neck. His shyness did not allow him to speak easily at professional meetings, but in smaller gatherings there was much to learn from his very wide and acutely remembered experience.

His was the sort of personality that throve, developed, and made an impact on the life of the hospital. Operating, teaching, in the wards most days and often at night for emergencies, he was there and seen to be there. He drove himself hard in his younger days and expected and got hard service from his juniors. Conscientious himself, he did not hesitate to castigate sloth, but he was generous to anyone who tried, and his example led many to try hard. In his later years, some of his apparent fierceness—and it was only apparent—mellowed, though his energy diminished not at all and he continued to get through an immense amount of work. His old students will long recount to each other tales of his mannerisms, his laughter, his abruptness, his energy. Bill was a very real man, and, now in their middle age, those former students will realise again how much they owe to him, from whom they learned their art and in whom they saw an example of the duty the doctor owes his patients and his work.

Mr. Williams leaves a widow and three sons, two of whom are doctors.

A memorial service will be held in St. Pancras Church, Euston Road, N.W.1, at noon on Monday, Feb. 17.

Mr. KENNETH BOWES

A. G. M., who was one of his students, writes:

The most obvious of Mr. Bowes' many outstanding qualities was his kindliness. He had the gift of always saying the right thing at the right moment, so that everyone felt at ease in his presence. His exceptional intellectual power and honesty gave him brilliant judgment, and, coupled with a delightful sense of humour, made him an inspiring teacher. He never taught at the bedside. The reason for this, he explained, was that on one occasion he was describing what it felt like to produce a baby when the patient looked up and said: " Sez you." This so shamed him that thereafter he met his class in the sideward, where he taught us a great deal of midwifery and gynæcology. Among his most popular stories were those of " patients who have caught me out ", and the favourite of all was of " the patient who caught me out twice ".

Diary of the Week

FEB. 16 TO 22

Monday, 17th

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Mr. Murray Falconer: Temporal Lobe Epilepsy.

HUNTERIAN SOCIETY
8.30 P.M. (Mansion House, E.C.4.) Dr. Macdonald Critchley: Animal Communication.

Tuesday, 18th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. Paul Fourman: Potassium Depletion.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. Dr. J. M. Holmes: Breech Presentation and Delivery.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Mr. A. T. Gray: Ointment Bases.

UNIVERSITY OF ST. ANDREWS, Queen's College, Dundee
5 P.M. Dr. R. P. Cook: Investigation of the Lipids.

Wednesday, 19th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Comparative Medicine.* Dr. W. F. H. Jarrett, Dr. W. I. M. McIntyre, Dr. W. Mulligan, Dr. F. Jennings, Dr. G. M. Urquhart, Dr. J. K. Walley, Dr. O. D. Standen: Recent Progress in Treatment and Prevention of Helminth Infections.
8.15 P.M. *General Practice.* Dr. R. M. McGregor, Dr. J. G. Ollerenshaw: Emergencies in General Practice.

POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. Rosemary Biggs: Blood Coagulation Factors in Theory and Practice.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Basal Cell Epitheliomata.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. E. H. Hudson: Use of Cortisone in Pulmonary Tuberculosis.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY
8 P.M. (Star and Garter Hotel, Putney Bridge, S.W.15.) Dr. R. D. Teare: Role of the Pathologist in the Investigation of Crime.

BIRMINGHAM MEDICAL INSTITUTE, Highfield Road, Edgbaston
8 P.M. *Psychiatry.* Dr. J. L. Clegg, Dr. R. J. Stanley: Report of the Royal Commission on the Law Relating to Mental Health.

NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY, 64, St. James's Street, Nottingham
8.30 P.M. Prof. R. J. V. Pulvertaft: Cinemicrography in Diseases of the Blood and Lymph Nodes.

Thursday, 20th

UNIVERSITY COLLEGE LONDON, Gower Street, W.C.1
5 P.M. Dr. F. H. C. Crick: The Nucleic Acids—Function. (Second of three lectures.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Prof. P. L. Krohn: Processes of Ageing in the Reproductive System.

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Dr. G. M. Ardran, Dr. F. H. Kemp: Radiological Investigation of Infant Feeding.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Prof. B. S. Platt: Malnutrition and Pathogenesis of Zymotic Diseases.

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford
8.30 P.M. Dr. G. N. C. Crawford: Growth of Muscle.

MANCHESTER MEDICAL SOCIETY
8 P.M. (Staff House, University of Manchester.) *Anæsthetics.* Dr. H. J. Brennan: Terminal Apnœa.

Friday, 21st

ROYAL SOCIETY OF MEDICINE
5 P.M. *Epidemiology and Preventive Medicine.* Dr. E. J. L. Lowbury, Dr. J. B. Selkon, Dr. H. Williams Smith: Epidemiological Risks of Antibiotics.
8.15 P.M. *Radiology.* Dr. Gordon Osborne, Dr. J. N. Pattinson: Benign Lesions of the Pyloric Antrum Simulating Carcinoma. Dr. Benjamin Green, Dr. R. A. Kemp Harper: Radiological Diagnosis of Malignant Gastric Ulcer. Dr. L. S. Carstairs: Headache and Gastric Emptying Time.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, Denmark Hill, S.E.5
4.30 P.M. Prof. Robert McWhirter: Recent Advances in Breast Cancer. (Dorothy Platt lecture.)

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. I. H. Griffiths: Incontinence of Urine.
4 P.M. Dr. A. G. MacGregor: Idiopathic Hæmochromatosis.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Mr. Wallace Black: Chronic Ulcers in the Mouth and Pharynx.
5.30 P.M. Dr. T. V. L. Crichlow: Radiology of the Temporal Bone

FACULTY OF RADIOLOGISTS
4.15 P.M. (Royal College of Surgeons, Lincoln's Inn Fields, W.C.2) Dr. George Ansell: Radiological Findings in Patients Treated with Cortisone and A.C.T.H.

Notes and News

CONGRESSIONAL COMMITTEE ON FALLOUT

IN May and June last year, the special subcommittee on radiation of the United States Congress joint committee on atomic energy heard evidence on the nature of radioactive fallout and its effects on man; and the proceedings have been published verbatim with many appendices, including the Medical Research Council report *The Hazards to Man of Nuclear and Allied Radiations* and many other reports, symposia, and statements. This abundant source of material for reference is published by the United States Government Printing Office in Washington, in two parts, with a total of 2055 pages. There is no index.

WHAT TO DO WITH SPUTUM

IN the prevention of spread of tuberculosis, safe disposal of the sputum of patients is extremely important. Those who have to care for tuberculous patients, whether in institutions or at home, will welcome a pamphlet [1] published by the Joint Tuberculosis Council. It describes the types of container and handkerchief (and handkerchief pocket) that are suitable, and the ways of destroying or effectively disinfecting them; 'Polythene' flasks, in which the sputum can be treated with a hypochlorite solution, are recommended. The pamphlet also gives advice to those who have to collect sputum containers, and the addresses of the manufacturers of all the equipment discussed.

University of Glasgow

On Jan. 25 the degree of M.D. was conferred on A. R. W. Climie (in absentia).

Royal College of Physicians of London

Dr. Charles Newman will give an "Unofficial FitzPatrick lecture" at the college on Friday, Feb. 28, to a meeting of members.

The meeting is open only to members, who may bring their wives to the lecture and to the sherry party to be held immediately after. Tickets are needed for the sherry party and can be had from the secretary of the college, Pall Mall East, S.W.1, not later than Feb. 17.

Royal College of Surgeons of England

The honorary fellowship has been conferred on Prof. Warren H. Cole (Chicago), Prof. Clarence Crafoord (Stockholm), Prof. F. L-P. de G. d'Allaines (Paris), Prof. C. F. W. Illingworth (Glasgow), Dr. Charles W. Mayo (Minnesota), and Prof. Herbert Olivecrona (Stockholm).

Royal College of Physicians of Edinburgh

At a meeting of college on Feb. 4 with Dr. A. Rae Gilchrist, the president, in the chair, the following were elected to the membership:

M. M. El-Nahas, Wilhelm Horovitz, S. N. Basu, Subramoney Nadarajah, Gopala Kuppuswamy, R. N. Dutta, F. E. Abdel-Gadir, C. P. Lowther, J. N. Wattie, A. M. I. Wasfi, W. J. Gomes, G. R. Sparrow, M. W. Partington, Ivan Hyde, Harry Coll, M. N. Khan, R. A. Papworth, Ramachandra Pararajasegaram, J. F. Moodie, N. J. W. Royston, Shih Chang Hu, A. L. Hilton, Shishu Pal Ram, G. B. Jain, Kamla Gupta, B. W. Cromie, B. K. Ahuja, R. A. Harkness.

James Yearsley Lecture

Mr. Francis McGuckin will give this lecture at the Royal Society of Medicine, 1, Wimpole Street, London, W.1, on Friday, March 7, at 5.15 P.M. His subject will be recent developments in tympanoplastic surgery.

Royal Commission on Remuneration

The Royal Commission on Doctors' and Dentists' Remuneration will hold a public hearing on Thursday, Feb. 20, at 11.15 A.M., at 10, Carlton House Terrace, London, S.W.1. Representatives of the General Practice Reform Association have been invited to attend.

1. Joint Tuberculosis Council: Report of the Public Health Committee on Collection and Sterilisation of Tuberculous Sputum in Hospital and at Home. Copies obtainable without charge and post free from Dr. R. L. Midgley, Hawkmoor Chest Hospital, Bovey Tracey, Devon.

Rockefeller Foundation

During the last quarter of 1957 the Foundation distributed over $19 million. Grants for medical education and public health amounted to some $3 million, and for biological and medical research to $2½ million.

Noxious Effects of Low-level Radiation

A symposium on this subject will be held in Lausanne from March 27 to 29. The speakers will include Dr. W. G. Marley, Dr. W. M. Court Brown, and Dr. N. Stewart. Further particulars may be had from the secretary, Schweizerishe Akademie der Medizinischen Wissenschaften, Petersplatz 13, Basle, Switzerland.

Merseyside Medical Art Society

This society, which was founded last year, is holding an inaugural dinner in Liverpool on April 2, to be followed by an exhibition which will be open to the public.

The president is Prof. B. G. Maegraith, and membership is open to any doctor resident on Merseyside and environs. Further particulars may be had from the secretary, Dr. D. B. Mossman, pathology department, Warrington General Hospital.

French Scientific Films

The films to be shown at the Institut Français, Queensberry Place, London, S.W.7, on Wednesday, Feb. 26, at 8.30 P.M., will include films on the role of the larynx in voice production, circulation in the pulmonary alveoli, and the physical and social reablement of accident cases. Tickets may be had from the scientific office, French Embassy, 22, Wilton Crescent, S.W.1.

An Eli Lilly medical research fellowship ($3600 per annum) is open to South African doctors who wish to do research in the United States. Further details can be had from Dr. H. Shapiro, P.O. Box 1010, Johannesburg. The closing date for applications is April 30.

On Tuesday, Feb. 25, at 5.30 P.M., at the Fountain Hospital, Tooting Grove, London, S.W.17, Dr. L. Fisch will give a lecture on the differential diagnosis of deafness and mental deficiency.

Nursing and Midwifery is the latest booklet in the Central Youth Employment Executive's Choice of Careers series. It may be obtained from H.M. Stationery Office and costs 1*s.* 9*d.* A companion booklet, *Nursing for Men*, will be published later this year.

The second edition of the *UFAW Handbook on the Care and Management of Laboratory Animals* can now be had from the Universities Federation for Animal Welfare, 7a, Lamb's Conduit Passage, London, W.C.1 (pp. 920. 70*s.*).

Appointments

BOWIE, A. T., M.B. Glasg.: assistant M.O.H., assistant school M.O., Dumfriesshire.
BRIDGE, A. J., M.R.C.S., F.D.S.: consultant dental surgeon, Guy's Hospital, London.
SHORT, I. A., M.B. Glasg., M.R.C.P., F.R.F.P.S.: part-time consultant physician, Western Infirmary, Glasgow.
SYKES, BLANCHE, M.R.C.S., D.P.H.: assistant M.O. (maternal and child welfare), Northumberland.

Manchester Regional Hospital Board

FERGUSON, R. S., M.D. Glasg., D.P.M.: consultant psychiatrist and medical superintendent, Lancaster Moor Hospital.
FIRTH, JOSEPH, M.B. Leeds, M.R.C.O.G.: part-time consultant obstetrician and gynæcologist, Bolton and district hospitals.
GOLDBERG, I. J. L.: B.SC. South Africa, M.R.C.S.: assistant pathologist, Oldham and district hospitals.
WILLIAMS, R. G., M.B. Lond.: assistant chest physician, Wigan and Leigh and Wrightington hospitals.

Births, Marriages, and Deaths

BIRTHS

GRIFFITHS.—On Jan. 31, to Barbara and Glyn Griffiths, M.B., of 179, East Dulwich Grove, S.E.22—a son, Charles William, brother for Mary Anne and Caroline.

DEATHS

BINGHAM.—On Feb. 4, Raymond Glendon Bingham, M.R.C.S., formerly of Garden House, Limes Avenue, Alfreton.

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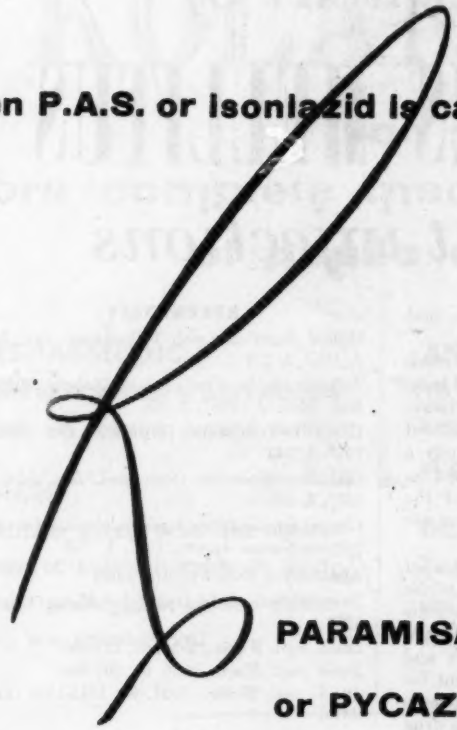

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Each tablet contains 0.5 G. of N-Butyl-N¹-toluene-p-sulphonylurea; (Tolbutamide).

REFERENCES:

Clinical Experience with Tolbutamide, *Brit. Med. J.*, 1957, **2**, 323

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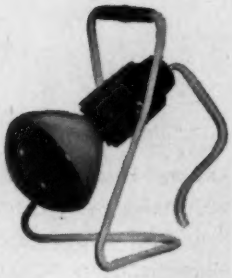

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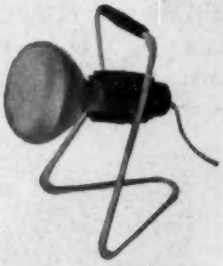

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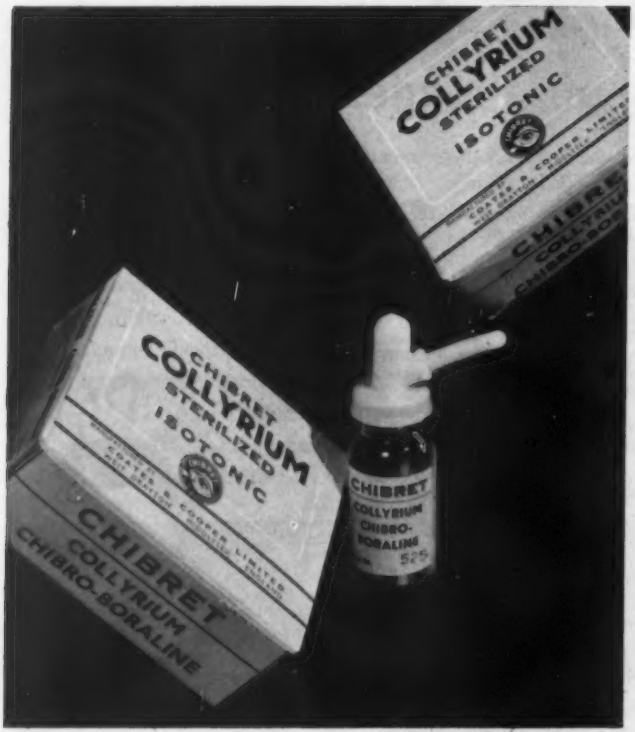

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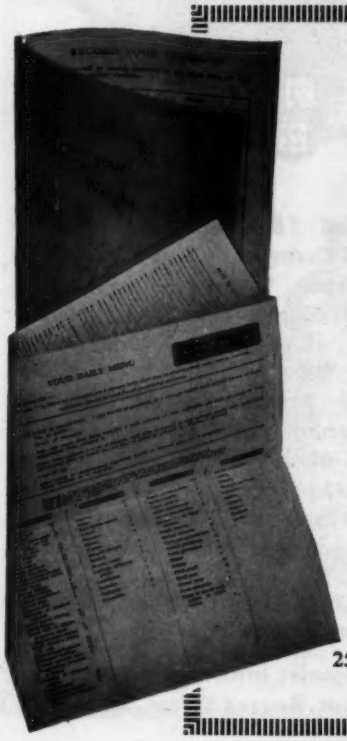

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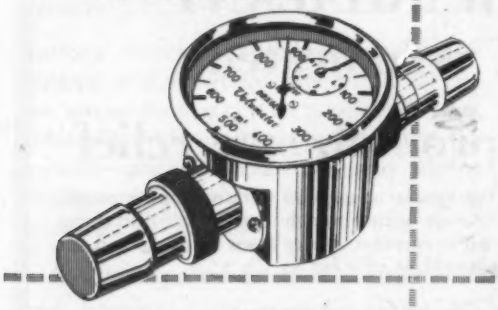

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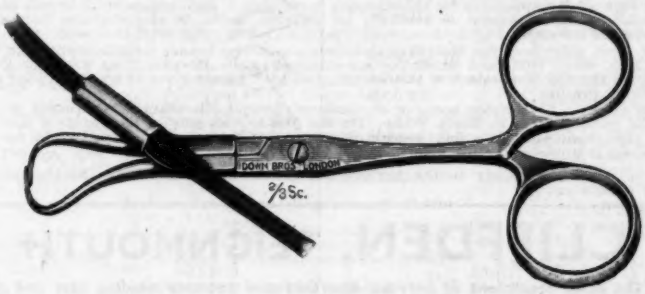

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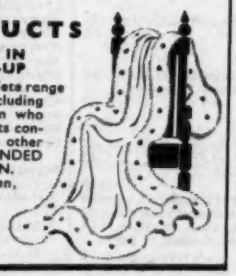

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ROCKEFELLER TRAVELLING FELLOWSHIPS IN MEDICINE

The Medical Research Council invite applications for the Rockefeller Travelling Fellowships in Medicine for the academic year 1958–59. These Fellowships are provided from a fund with which the Council have been entrusted by the Rockefeller Foundation of New York. They are intended for graduates resident in this country who have had some training in research work in clinical medicine or surgery, or in some other branch of medical science, and who are likely to profit by a period of work at a centre in the United States or elsewhere abroad, before taking up appointments for higher teaching or research in the United Kingdom.

Fellowships tenable in the United States will normally provide a maintenance allowance at the rate of $3000 p.a. for a single Fellow and $4200 p.a. for a married Fellow. Provision will be made for the Fellow's own travelling and other approved expenses, and a small family allowance will also be available.

Further particulars of these Fellowships and forms of application may be obtained from the Secretary, Medical Research Council, 38, Old Queen-street, Westminster, S.W.1, with whom applications must be lodged not later than 1st March, 1958.

Applications should also be submitted to the Council by 1st March for a limited number of Lilly Foreign Fellowships, United States Public Health Service Fellowships, and a Lederle Fellowship, the terms of which resemble closely the Rockefeller Fellowships described above.

PADDINGTON GROUP HOSPITAL MANAGEMENT COMMITTEE

THE TAVISTOCK CLINIC

INTRODUCTORY COURSE ON PSYCHOLOGICAL PROBLEMS IN GENERAL PRACTICE

A course of 8–10 weekly discussion meetings for a limited number of general practitioners will start in APRIL on WEDNESDAYS 2–4 P.M., and another course in MAY on TUESDAYS 2–4 P.M. Admission is free.

Apply in writing to Medical Director, Tavistock Clinic, 2, Beaumont-street, W.1, stating course preferred.

TANCRED'S STUDENTSHIPS

DIVINITY: MEDICINE: LAW
£100 p.a. each. For men only

About WHITSUNTIDE next the Governors propose to elect 1 Student in Law at Lincoln's Inn. Candidates must have been born in England, Scotland or Wales and be members of the Church of England and unmarried.

Candidates must be within the ages of 20 and 23 years on the 1st October, 1958. The last day for sending in Petitions is the 11th March, 1958.

Further announcements relating to the Physic and Divinity Studentships awarded by this Foundation will appear in April and September, 1958.

Apply for further particulars and form of Petition stating kind of Studentship and mentioning this paper to the Clerk, R. M. C. HOWARD, Esq., D.S.O., 28, Lincoln's Inn-fields, London, W.C.2.

UNIVERSITY OF GLASGOW
and
ROYAL FACULTY OF PHYSICIANS AND SURGEONS

POSTGRADUATE MEDICAL EDUCATION COMMITTEE

CONFERENCE ON NEOPLASIA

A SPECIALIST CONFERENCE ON NEOPLASIA will be held in the Royal Faculty of Physicians and Surgeons, 242, St. Vincent-street, Glasgow, C2, from 26TH to 28TH of MARCH, 1958. The conference is open to all medical practitioners. The programme is as follows:—

		Speakers	*Chair*
Wednesday, 26th March, 1958			
9.45 A.M.	Inauguration		
10.00 A.M.	Fundamental Biology and Concepts of Neoplasia	J. N. DAVIDSON P. R. PEACOCK R. J. C. HARRIS (London)	Prof. S. ALSTEAD
2.00 P.M.	Endogenous Cancer	B. D. PULLINGER	Mr. ARTHUR JACOBS
2.45 P.M.	Occupational Cancer	A. T. DOIG	
Thursday, 27th March, 1958			
10.00 A.M.	Medical Problems in Neoplasia Hormones in Neoplasia	A. R. CURRIE R. I. SHAW DUNN A. BROWN	Prof. L. J. DAVIS
2.00 P.M.	(*a*) Breast cancer	A. P. M. FORREST	Prof. T. SYMINGTON
2.45 P.M.	(*b*) Prostatic malignancy	W. B. STIRLING	
Friday, 28th March, 1958			
	Regional Neoplasia		
10.00 A.M.	(*a*) Carcinoma of liver	J. W. ORR (Birmingham)	Prof. W. A. MACKEY
11.15 A.M.	(*b*) Carcinoma of stomach	C. F. W. ILLINGWORTH	
2.00 P.M.	(*c*) Carcinoma of thyroid	E. M. MCGIRR	Prof. E. J. WAYNE
2.45 P.M.	(*d*) Carcinoma of lung	R. S. BARCLAY	

There is no fee for the course. There will be an informal Conference Dinner on Thursday, 27th March, at 7.00 P.M. for 7.30 P.M. Tickets, inclusive of wine, are £1.

Further particulars may be had from the Registrar, Royal Faculty of Physicians and Surgeons, 242, St. Vincent-street, Glasgow, C.2.

ST. MARY'S HOSPITAL MEDICAL SCHOOL (University OF LONDON), Paddington, W.2. Applications are invited for the appointment of LECTURER IN MORBID ANATOMY for a period of 3 years from 1st April, 1958, or as soon as possible thereafter. Salary scale £1150–£100–£1750 together with superannuation and children's allowance. Considerable time available for experimental work.

Applications (2 copies), with the names of 3 referees, should be sent by 10th March, 1958, to the Secretary, St. Mary's Hospital Medical School, from whom further particulars may be obtained.

UNIVERSITY OF DURHAM. King's College, Newcastle UPON TYNE. The Council of King's College invite applications for the post of RESEARCH ASSISTANT in the Department of Anæsthetics. Candidates need not necessarily hold a medical qualification. Physiological knowledge and experience in simpler biochemical estimations would be of value. The salary will be in the range £700–£1200 with child allowance and F.S.S.U. benefits.

Applications, together with the names of 2 referees, should be submitted not later than Saturday, 1st March, 1958, to the undersigned. G. R. HANSON, Registrar of King's College.

UNIVERSITY OF EDINBURGH. Department of SURGICAL SCIENCE. Applications are invited for the post of IMMUNOLOGIST in the Department of Surgical Science, to work on problems of transplantation immunity under the general direction of the Professor. Applicants should be graduates in either science or medicine and have a sound knowledge of immunology. The successful applicant, who will be given the status of either Lecturer or Senior Lecturer, according to qualifications and experience, will be expected to give some postgraduate instruction in experimental methods and may also be called upon to supervise research students but will have no other teaching duties. If the person appointed is given the status of Senior Lecturer the salary scale will be £1950–£100–£2550 p.a.; if the status of Lecturer the scale will be £900–£100–£1300; bar: £1400–£100–£1900 with placement according to qualifications and experience. The post is subject to superannuation and family allowance is payable where applicable.

Further particulars may be obtained from the undersigned, with whom applications (6 copies), giving the names of 2 referees, should be lodged not later than 31st March, 1958.

CHARLES H. STEWART, Secretary to the University.
January, 1958.

THE INSTITUTE OF LARYNGOLOGY AND OTOLOGY
(UNIVERSITY OF LONDON)
330/332, Gray's Inn-road, London, W.C.1

COURSE ON THE DEAF CHILD for Physicians and Senior Registrars 29TH, 30TH APRIL and 1ST MAY, 1958.
Syllabus obtainable from the Dean.

THE UNIVERSITY OF MANCHESTER. Applications are invited for the full-time post of LECTURER IN OTO-LARYNGOLOGY. Salary on a scale rising to £2150 p.a. ; initial salary according to qualifications and experience. Membership of the F.S.S.U. and children's allowance scheme.
Applications should be sent not later than 28th February, 1958, to the Registrar, The University, Manchester, 13, from whom further particulars and forms of application may be obtained.

Hospital Services: Senior Appointments

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.
1. CONSULTANT PSYCHIATRIST-IN-CHARGE, 6 half-days a week, High Wick, Tyttenhanger, St. Albans, Herts (approximately 20 Beds for psychotic and maladjusted children 3–10 years old). Interest in research encouraged.
Applications before 17th March, 1958.
2. CONSULTANT RADIOLOGIST, 5 half-days a week, Ashford Hospital, Ashford, Middlesex (562 Beds) and Hounslow Hospital, Hounslow, Middlesex (81 Beds).
Applications before 21st March, 1958.
3. ASSISTANT PATHOLOGIST, whole-time, Senior Hospital Medical Officer grade, King Edward Memorial Hospital, Ealing, W.13, and associated hospitals. Duties include public health laboratory work and general practitioner service for surrounding area.
Applications before 19th March, 1958.
4. CONSULTANT RADIOLOGIST, whole-time or maximum sessions, Barnet General Hospital, Wellhouse-lane, Barnet, Herts (461 Beds). Department also responsible for the work of Victoria Maternity (59 Beds), St. Stephen's (88 Beds), and Potters Bar and District (56 Beds) Hospitals.
Applications before 28th March, 1958.
5. ASSISTANT NEUROSURGEON (Consultant grade), whole-time or maximum sessions, Central Middlesex Hospital, Acton-lane, N.W.10 (726 Beds). Successful candidate will be required to devote part of his time to work in the western part of the Region.
Applications before 24th March, 1958.
6. CONSULTANT E.N.T. SURGEON, 1 half-day a week, on Wednesday, Acton Hospital, Gunnersbury-lane, W.3 (84 Beds).
Applications before 26th March, 1958.
Unit and Hospitals may be visited by direct appointment.
Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

CANTERBURY AND ISLE OF THANET HOSPITAL MANAGEMENT COMMITTEES. Locum ANÆSTHETIST (Consultant or Senior Hospital Medical Officer grade) (full-time) immediately until the end of June, 1958. Duties in the above areas and required to reside in Thanet district. Car essential.
Applications to Group Secretary, Central Office, Nunnery Fields Hospital, Canterbury.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. ASSISTANT PSYCHIATRIST, St. Andrew's Mental Hospital Group, Norwich. Duties mainly at St. Nicholas Hospital, Great Yarmouth (formerly Gt. Yarmouth Naval Hospital), where a house is available. Salary scale £1653 15s.–£2126 5s.
Applications (8 copies), stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 3rd March, 1958. Candidates are invited to visit hospitals by direct arrangement with the Medical Superintendent, St. Andrew's Hospital, Thorpe, Norwich.

MANCHESTER REGIONAL HOSPITAL BOARD.
(*a*) Maximum Part-time CONSULTANT NEUROLOGIST to the Booth Hall (Children's) Hospital, Manchester, and the Royal Manchester Children's Hospital. The appointee will also be required to visit the David Lewis Epileptic Colony in Cheshire weekly and make regular weekly consultative visits to Preston. Wide experience and higher qualifications essential. 5th March, 1958.
(*b*) Whole-time NON-RESIDENT ASSISTANT RADIOTHERAPIST (Senior Hospital Medical Officer), Christie Hospital and Holt Radium Institute, Manchester. F.F.R. or other higher qualification desirable ; appointee to live in or near Manchester. 3rd March, 1958.
Application forms from the Senior Administrative Medical Officer of the Board at Cheetwood-road, Manchester, 8, to be returned by dates stated.

OXFORD REGIONAL HOSPITAL BOARD. Consultant RADIOLOGIST (whole-time or maximum part-time) to the hospitals of the Reading Area. The Consultant will share in the Radiological Service centred on the Royal Berkshire Hospital (338 Beds) with peripheral departments at 7 other hospitals. Applicants must hold the D.M.R. or equivalent and a higher qualification in medicine or surgery is desirable.
Applications (10 copies), stating age, qualifications, experience, and the names of 3 referees, should reach the Secretary, 43, Banbury-road, Oxford, by 10th March.

NEWCASTLE REGIONAL HOSPITAL BOARD. Consultant ANÆSTHETIST, whole-time or maximum part-time, for Hexham Group of hospitals—main hospital Hexham General (300 Beds); also duties at Prudhoe and Monkton Mental Diseases Hospital (1160 Beds).
Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Consultant ORTHOPÆDIC SURGEON, whole-time or maximum part-time, for Newcastle, South East Northumberland and Wansbeck Hospital Management Committee areas, and Hartford Hall Rehabilitation Centre.
Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time appointment of RESIDENT ASSISTANT PHYSICIAN (graded for the purposes of salary as Senior Casualty Officer), tenable at the Royal Victoria Infirmary. The appointment is for 1 year in the first instance and may be renewed to a maximum of 4 years. The successful candidate may have clinical responsibilities on one of the medical wards and will be responsible for the day-to-day supervision of the Casualty and Admissions Department. The appointment will be subject to the terms and conditions of service of hospital medical staff in the National Health Service.
Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.
A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.
Part-time CONSULTANT PSYCHIATRIST to Harlow (New Town) Child Guidance Clinic for 4 sessions a week. New clinic in developing area. Further particulars on application.
Full-time CONSULTANT PSYCHIATRIST to Runwell Hospital, near Wickford, Essex. Higher qualification desirable. Duties include clinics in Southend-on-Sea Group of hospitals. House available on Runwell estate.
Applications (6 copies) and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 15th March, 1958.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of CONSULTANT PHYSICIAN, 5 sessions per week, at the Longmore and Deaconess Hospitals, Edinburgh.
Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited from Women practitioners for the appointment of CONSULTANT PHYSICIAN, 5 sessions per week, at the Bruntsfield and Elsie Inglis Hospitals, Edinburgh.
Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited from Women practitioners for the appointment of MEDICAL PÆDIATRICIAN (Consultant), 2 sessions per week, at the Bruntsfield and Elsie Inglis Hospitals, Edinburgh.
Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited from Women practitioners for the appointment of DERMATOLOGIST (Senior Hospital Medical Officer), 1 session per week, at the Bruntsfield and Elsie Inglis Hospitals, Edinburgh.
Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT SENIOR CASUALTY OFFICER required at the County Hospital, Lincoln. Salary scale £1653 15s.–£52 10s.–£2126 5s. p.a. Tenure for a period not exceeding 4 years.
Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 17th March.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens CONSULTANT ORTHOPÆDIC AND TRAUMATIC SURGEON required, Clwyd and Deeside Hospital Management Committee area immediately.
Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Consultant E.N.T. SURGEON to Mid-Glamorgan Hospital Management Committee. Visits to Neath General, Bridgend General and other hospitals in the Group. Optional whole-time/maximum part-time appointment.
Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Welsh Regional Hospital Board, Temple of Peace, Cathays Park, Cardiff, within 21 days.

WELSH REGIONAL HOSPITAL BOARD. Consultant OPHTHALMOLOGIST to West Wales Hospital Management Committee area. Based on West Wales General Hospital, Carmarthen. Optional whole-time/maximum part-time appointment.
Applications (12 copies), naming 3 referees, to Senior Administrative Medical officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

Hospital Services: Junior Appointments

BATTERSEA GENERAL HOSPITAL, Battersea Park, S.W.11. HOUSE SURGEON/CASUALTY OFFICER. Combined post. Resident. Vacant immediately. House Officer grade, not pre-registration and not recognised for F.R.C.S.
Apply, enclosing copies of 2 recent testimonials, to Hospital Secretary, with whom arrangements can be made to view the Hospital.

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. HOUSE SURGEON, resident. Vacant 29th March, 1958. Open to registered practitioners and pre-registration candidates.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 24th February, 1958.

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. Locum HOUSE SURGEON, 15th–28th March, 1958.

Apply Hospital Secretary. Phone BATtersea 2445.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in Orthopædic and Traumatic Department. Post vacant 22nd February.

Applications, with 2 testimonials, to Medical Director immediately.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. SENIOR HOUSE OFFICER required in the Pathology Department. Good training in all branches of pathology. Recognised for Diploma in Pathology. Hospital may be visited by arrangement. Position vacant 2nd April, 1958.

Applications, with names 2 referees, to Medical Director by 22nd February, 1958.

CHILDREN'S HOSPITAL, Sydenham, S.E.26. (100 Beds.) SENIOR RESIDENT MEDICAL OFFICER (Senior House Officer) required 1st April for 1 year. Duties include Medicine and Surgery. Recognised for D.C.H. Previous pædiatric experience essential.

Apply, naming 2 referees, to Administrative Officer by 21st February.

DULWICH HOSPITAL, East Dulwich-grove, S.E.22. HOUSE SURGEON (general surgical duties) required from 1st March. Recognised pre-registration post.

Apply, giving age, qualifications and experience (if any) with copy testimonials or names of 2 referees, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, as soon as possible.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from registered Women medical practitioners for the post of RESIDENT PATHOLOGIST. Salary in accordance with Ministry of Health scale for Senior House Officers. The appointment is for 6 months in the first instance. Duties to commence 1st April, 1958.

Applications, with copies of 3 recent testimonials, should be sent to The Secretary, Elizabeth Garrett Anderson Hospital, by 19th February.

GUY'S HOSPITAL, S.E.1. Applications are invited for the post of REGISTRAR (mid-grade) in the Department of Clinical Pathology, with duties from 17th March, 1958, until 30th September, 1959, in the first instance.

Forms of application are obtainable from, and should be lodged with, the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 28th February, 1958.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Joint appointment with the North West Metropolitan Regional Hospital Board. Whole-time REGISTRAR (orthopædic) required. Post vacant now. Appointment tenable firstly at Heatherwood Hospital, Ascot (resident if required), studying long-term orthopædic surgery, transferring to Hammersmith Hospital and the Postgraduate Medical School (non-resident) on 1st August, 1958, studying orthopædic and traumatic surgery.

Applications, stating age, qualifications, experience, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London, and St. Mark's Hospitals, Ducane-road, London, W.12. by 22nd February.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Applications invited for following whole-time, non-resident posts:

SENIOR REGISTRAR (general surgery).

REGISTRAR (general surgery).

Applications, stating age, qualifications, experience, names 2 referees, to Secretary, The Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, 150, Ducane-road, London, W.12, by 28th February.

HAMPSTEAD GENERAL HOSPITAL, Haverstock Hill, N.W.3. ROYAL FREE HOSPITAL GROUP. Applications are invited from registered medical practitioners for the post of RESIDENT CASUALTY OFFICER (graded as Senior House Officer). Salary £745 p.a. Tenable for a period of 6 months from 1st April, 1958, at the Main Outpatient Department, Bayham-street, N.W.1.

Application forms may be obtained from the Secretary, to whom they should be returned, together with copies of 3 recent testimonials, by 27th February, 1958.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. ANÆSTHETIST (Senior House Officer grade), resident, 12 months' appointment. Vacant 8th March. 100 active surgical and orthopædic beds. Approximately 1200 operations annually.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE PHYSICIAN, vacant 27th February, 1958. Preference given to applicants seeking pre-registration post under Medical Act, 1950.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

KING'S COLLEGE HOSPITAL, Denmark-hill, S.E.5. Applications are invited for the post of REGISTRAR to the X-ray Diagnostic Department. Candidates should hold or intend to work for a Diploma in Radiology. The post is tenable from 1st April, 1958, until 30th September, 1958, in the first instance, and is thereafter renewable annually.

Applications, stating age, education, qualifications and experience, together with the names of 2 referees, should be sent to the undersigned by 1st March, 1958.

S. W. BARNES, House Governor.

LAMBETH HOSPITAL, Brook-drive, S.E.11. South West METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the post of RESIDENT OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR, vacant now. The appointment is normally for 2 years, subject to annual review. The post is recognised for the M.R.C.O.G. and includes some teaching of medical students from St. Thomas's Hospital. Candidates may visit the Hospital.

Forms of application, from the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, should be returned by 1st March, 1958.

LONDON CHEST HOSPITAL (Country Branch). HosPITALS FOR DISEASES OF THE CHEST. REGISTRAR in Clinical Pathology (Registrar grade). A vacancy occurs at the country branch near Letchworth. The appointment is a whole-time one and will be for 1 year in the first instance and the holder may be resident or non-resident.

Applications, stating age, qualifications with dates, and previous experience, together with copies of 3 testimonials, should reach the House Governor, London Chest Hospital, E.2, not later than 22nd February, 1958.

LONDON CHEST HOSPITAL. Hospitals for Diseases of THE CHEST. 2 vacancies occur 1st April, 1958, for RESIDENT HOUSE PHYSICIAN. Appointments for 6 months, 4 in London, 2 at the Country Branch, near Letchworth, and posts graded as House Officer. Duties include work in the Outpatient Department and special clinics, as well as in wards.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the House Governor, London Chest Hospital, E.2, not later than 1st March, 1958.

MILE END HOSPITAL, Bancroft-road, London, E.1. (484 Beds.) HOUSE PHYSICIAN (pre- or post-registration). Post vacant 8th March, 1958.

Application forms, obtainable from Physician-Superintendent, to be returned by 21st February, 1958, with copies of not more than 3 testimonials.

NATIONAL HEART HOSPITAL, Maids Moreton, BuckINGHAMSHIRE. (Country Branch of the National Heart Hospital.) Applications are invited for the post of RESIDENT MEDICAL OFFICER at the Hospital's country branch. The appointment is for a period of 5 months from 1st May, 1958, but may be renewed for a further period not exceeding 6 months. The status of the post is that of a Senior House Officer, and the salary is in accordance with the terms and conditions of service. The holder will be expected to attend on 1 day weekly at the Hospital in Westmoreland-street.

Applications, with copies of 3 recent testimonials, should be sent to me at Westmoreland-street, London, W.1, not later than 28th February, 1958.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL HEART HOSPITAL, Westmoreland-street, W.1 (with which is associated the Institute of Cardiology). REGISTRARS. The Board of Governors invites applications to fill 2 vacancies, 1 as from 1st April and the other as from 1st May, 1958. Applicants should have been fully trained in general medicine and should possess a higher medical qualification. Opportunities for research available.

Applications, with copies of 3 recent testimonials, should be sent to me not later than Friday, 28th February, 1958.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL HEART HOSPITAL, Westmoreland-street, W.1 (with which is associated the Institute of Cardiology). Applications are invited for the post of ASSISTANT RESIDENT MEDICAL OFFICER (Male). The appointment is for a period of 6 months from 1st April, 1958, but may be renewed for a further period of 6 months. The status and salary are those of a Senior House Officer in accordance with the national terms and conditions of service.

Applications, with copies of 3 recent testimonials, should be sent to me not later than Friday, 28th February, 1958.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL TEMPERANCE HOSPITAL, Hampstead-road, N.W.1. (General Hospital of 158 Beds.) Applications are invited to fill the post of HOUSE SURGEON (general), pre-registration post. Vacant 5th March, 1958. Applications by post-registration candidates will also be considered.

Applications, stating age, qualifications, experience, together with the names and addresses of 2 referees, to be forwarded to Hospital Secretary by 21st February, 1958.

NORTH MIDDLESEX HOSPITAL, London, N.18. House PHYSICIAN, post-registration, resident, required for 1st April, for 6 months. General medicine.

Applications (in own handwriting), stating age, nationality, qualifications, experience, with copies of recent testimonials, to Hospital Secretary, by 18th February.

NORTH MIDDLESEX HOSPITAL, London, N.18. Senior HOUSE OFFICER in Surgery, resident, required. General surgery, trauma and orthopaedics. Post recognised for F.R.C.S. 6 months' appointment in the first instance, with possible extension to 1 year. Vacant 1st April.

Applications, stating age, nationality, qualifications (Primary Fellowship desirable), experience, with copies of recent testimonials and/or names of 2 referees, to Hospital Secretary, by 18th February.

ROYAL FREE HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR CASUALTY OFFICER at the Royal Free Hospital, Gray's Inn-road, W.C.1. The appointment is full-time, resident, for 6 months, duties to commence on 1st April, 1958. Salary and conditions of service in accordance with those laid down by the Ministry of Health for Senior House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 19th February, 1958.

ROYAL FREE HOSPITAL. Applications are invited for the post of JUNIOR RESIDENT ANÆSTHETIST. The appointment is for 6 months, duties to commence 1st April, 1958. Salary in accordance with the Ministry of Health scale for House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 19th February, 1958.

ROYAL FREE HOSPITAL. Applications are invited for the post of SENIOR RESIDENT ANÆSTHETIST. The appointment is for 6 months, duties to commence 1st April, 1958. Salary in accordance with the Ministry of Health scale for House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 19th February, 1958.

ROYAL EYE HOSPITAL, St. George's-circus, London, S.E.1. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER from 1st April, 1958. The Hospital is recognised for F.R.C.S. and D.O. examinations.

Request for application form to be made to the Hospital Secretary, to be returned not later than 24th February, 1958.

ROYAL EYE HOSPITAL, St. George's-circus, London, S.E.1. Locum SENIOR HOUSE OFFICER for holiday periods prior to 31st March, 1958.

Applications to the Secretary (WATerloo 4477) immediately.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, Brockley Hill, STANMORE, MIDDLESEX. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (2 vacancies) for a period of 6 months. Duties to commence on 8th April, 1958, and 13th May, 1958.

Applications to be received by 12th March, 1958. Forms of application can be obtained from the House Governor at 234, Great Portland-street, London, W.1.

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1, with which is associated the Institute of Laryngology and Otology (University of London). GENERAL PRACTITIONER CLINICAL ASSISTANTS and OUTPATIENT ASSISTANTS. These appointments give those engaged in general practice who are able to attend for 2 sessions weekly over a period of 15 months commencing in March, 1958, the opportunity of widening their clinical experience in the specialty. At the end of 3 months' training period the holders will be appointed as Outpatient Assistants with remuneration under paragraph 10 (b) of the National Health Service terms and conditions of service.

Further particulars may be obtained from the House Governor.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (pathology) for Group Laboratory, vacant 24th March, 1958.

Applications to be sent to the Hospital Secretary by 1st March, 1958.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered Female medical practitioners for the post of Resident Full-time OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR. Vacant 24th April, 1958. Appointment recognised for M.R.C.O.G. as combined appointment, normally for 2 years. Canvassing will disqualify but candidates not precluded from visiting Hospital if they so desire.

Forms of application (enclosing self-addressed envelope) from the Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to whom completed applications should be returned not later than 1st March, 1958.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited from pre-registration and registered Female medical practitioners for the appointment of OBSTETRIC HOUSE SURGEON. Recognised for the M.R.C.O.G. Appointment for 6 months from 24th April, 1958.

Forms of application from the Secretary.

ST. GILES' HOSPITAL, Camberwell, S.E.5. House SURGEON (orthopædic duties) required. Pre- or post-registration post.

Apply, giving age, qualifications and previous posts (if any), with copy testimonials or names of 2 referees, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, S.E.22.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. Senior HOUSE OFFICER (anæsthetics). Post recognised for D.A. and F.F.A. R.C.S. Vacant 1st March.

Applications, stating age, qualifications, experience, and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (General—192 Beds.) Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE PHYSICIAN for 6 months.

Applications, with 2 recent testimonials, to be sent to the Hospital Secretary by 1st March, 1958. Applications may be sent in pending the qualifying examination results being known, and provided these are available at the date of interview.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be vacancies on 15th May, 1958, for the following Senior House Officers:—

A HOUSE PHYSICIAN
A HOUSE SURGEON
to the Orthopædic and Plastic Departments.

Further particulars and forms of application, which must be returned not later than 10th March, 1958, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. House SURGEON. Vacant now. Recognised for F.R.C.S. and approved for pre-registration service.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the post of ASSISTANT BACTERIOLOGIST in the Department of Clinical Pathology (graded Junior Hospital Medical Officer). Experience in pathology desirable.

Applications, with names of 2 referees, to T. F. W. MACKEOWN, Administrator and Secretary, by 26th February, 1958.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the post of JUNIOR RESIDENT ANÆSTHETIST (graded Senior House Officer) for a period of 6 months from 1st March, 1958.

Written applications, with the names of 2 referees, to T. F. W. MACKEOWN, Administrator and Secretary, by 28th February, 1958.

WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.) HOUSE SURGEON required. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WEST LONDON HOSPITAL, Hammersmith-road, London, W.6. Whole-time NON-RESIDENT REGISTRAR (general medicine) required, mid-April.

Applications, stating age, qualifications, experience, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 24th February.

WHIPPS CROSS HOSPITAL, Leytonstone, E.11. LEYTONSTONE (NO. 10) HOSPITAL GROUP. Applications are invited for the post of PÆDIATRIC HOUSE PHYSICIAN (post-registration) at above Hospital. The post, which is recognised for D.C.H., becomes vacant on 1st April, 1958.

Application forms obtainable from the Hospital Secretary, to be returned by 24th February, 1958.

ALTON GENERAL HOSPITAL, Alton. (136 Beds. Acute general.) RESIDENT HOUSE SURGEON required for general surgical duties. Vacant immediately. Recognised for F.R.C.S. 6 months' appointment.

Applications and copies of testimonials to be sent to the Hospital Secretary.

ASCOT. HEATHERWOOD ORTHOPÆDIC HOSPITAL. Locum REGISTRAR (orthopædics) required first 2 weeks in March.

Applications, giving full details of experience and names of 2 referees, to Secretary.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required to assist Consultant Geriatrician in a modern unit which serves the area of the Hospital Management Committee, with main duties at Ashton-under-Lyne General Hospital. There is full scope for the study of clinical medicine and the post is suitable for a young physician wishing to work for higher qualifications or interested in social medicine and rehabilitation.

Applications, together with 2 references, to the Group Secretary, General Hospital, Ashton-under-Lyne.

AYLESBURY, BUCKINGHAMSHIRE. STOKE MANDEVILLE HOSPITAL. (619 Beds.) Applications are invited for the post of RESIDENT HOUSE PHYSICIAN in the Department of Medicine. Pre-registration post but registered practitioners may apply. Duties include responsibility for 20 acute medical beds and 15 tuberculosis beds. Post vacant early March.

Applications, with copies of 2 testimonials, to the Administrative Officer by 19th February. Interview 26th February.

AYLESBURY. ROYAL BUCKINGHAMSHIRE HOSPITAL. Locum CASUALTY OFFICER (Senior House Officer) for period 7th–21st March.

Apply, with copies of 2 recent testimonials, to Secretary-Superintendent as soon as possible.

BEBINGTON, CHESHIRE. CLATTERBRIDGE HOSPITAL. CENTRAL WIRRAL GROUP.

HOUSE OFFICER (general medicine and geriatrics). Recognised pre-registration.

HOUSE OFFICER (general surgery). Recognised pre-registration.

Posts are tenable for 6 months from 1st March, 1958. Salary according to previous posts held.

Application forms, from Secretary, to be returned by 20th February, 1958.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE PHYSICIAN. Resident pre-registration post, available on 2nd April, 1958, in the Department of Medicine.

Applications, stating age, experience (if any) and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL VICTORIA HOSPITAL. Casualty Officer (Junior Hospital Medical Officer). This post vacant on 1st March is recognised for the F.R.C.S. and offers a variety of experiences in a busy department. Residence is optional. Minimum tenure of 1 year. Salary £852 10s.–£55–£1182 10s.

Applications, stating age, qualifications, experience and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BODMIN, CORNWALL. ST. LAWRENCE'S HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER, to become available on 1st April, 1958, at the above Mental Hospital of 1250 Beds. National Health Service salary (£852 10s. p.a.–£55(6)–£1182 10s. p.a.) and conditions. Incremental concessions for special experience or qualifications. Residential accommodation for single man.

Applications, giving full details and names and addresses of 3 referees, to be sent to the Group Secretary, St. Lawrence's Hospital, Bodmin, as soon as possible.

BARROW-IN-FURNESS. DEVONSHIRE ROAD HOSPITAL. Applications are invited for the resident post of SENIOR HOUSE OFFICER (pædiatrics) for the Pædiatric Unit at the above Hospital. The post, which is available at the end of April, provides good inpatient and outpatient experience in pædiatrics, and will also include the care of a ward for medical cases (adults) and infectious diseases (children and adults).

Applications, giving age, qualifications and experience, and names of 2 referees, to the Group Secretary, Barrow and Furness Hospital Management Committee, 105, Abbey-road, Barrow-in-Furness.

BARROW-IN-FURNESS. NORTH LONSDALE HOSPITAL. Applications are invited for the resident posts of SENIOR HOUSE OFFICER (surgical) and HOUSE OFFICER (surgical) at the North Lonsdale Hospital, Barrow-in-Furness. Both posts are recognised for F.R.C.S., and are available at the beginning of March and immediately, respectively. The latter post is approved for pre-registration service.

Applications to Group Secretary, Barrow and Furness Hospital Management Committee, 105, Abbey-road, Barrow-in-Furness.

BIRMINGHAM. MOSELEY HALL HOSPITAL FOR CHILDREN, Alcester-road, BIRMINGHAM, 13. (65 Beds.) SENIOR HOUSE OFFICER (pædiatric). Vacant March. Resident/non-resident. Recognised for D.C.H.

Apply, with 3 testimonials, by 22nd February, to Secretary, Birmingham (Selly Oak) Hospital Management Committee, Oak Tree-lane, Birmingham, 29.

BIRMINGHAM (near). MARSTON GREEN MATERNITY HOSPITAL, Berwicks-lane, MARSTON GREEN, near BIRMINGHAM. RESIDENT SENIOR HOUSE OFFICER in Pædiatrics required for 6 months or 1 year (the latter to be recognised for D.C.H.). Duties in Premature Baby Unit (12 Cots); in Neonatal Department at above Hospital (121) (Hospital affiliated to the University of Birmingham for the teaching of students), and in neonatal and Children's Departments at neighbouring hospitals. Previous pædiatric or obstetric experience desirable.

Detailed applications to the Group Secretary, Dudley Road Hospital, Birmingham, 18, not later than 20th February, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE BIRMINGHAM MATERNITY HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT OBSTETRIC HOUSE SURGEON, vacant 1st May, 1958. The appointment is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms obtainable from the House Governor, the Birmingham and Midland Hospitals for Women, Showell Green-lane, Sparkhill, Birmingham, 11, to be returned not later than 3rd March, 1958. G. A. PHALP, Secretary.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of REGISTRAR in Pathology. The successful candidate will take part in a training scheme to be instituted in collaboration with the division of pathological studies, University of Birmingham, providing for experience in all branches of pathology and work in various specialised hospitals within the United Hospitals.

Further information concerning the appointment, and forms of application, may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned by 28th February, 1958.

BOGNOR WAR MEMORIAL HOSPITAL. (32 Beds.) RESIDENT SENIOR HOUSE OFFICER required to work under visiting Consultant Surgeon and Physician; also casualty work. Salary £819 10s. less £150 p.a. for residence. Modern fully-equipped theatre. Good liaison with Chichester main hospitals and with local practitioners. Also gives opportunity for post-graduate reading.

Apply, giving 3 referees' names, to Group Secretary, Chichester Group Hospital Management Committee, 174, Broyle-road, Chichester.

BRIGHTON. SUSSEX EYE HOSPITAL. (56 Beds.) HOUSE SURGEON required early March. Recognised for F.R.C.S. and D.O. Successful candidate will be considered for senior post (Senior House Officer) on completion of 6 months.

Applications, stating age, qualifications and experience and naming 2 referees, to the Administrative Officer.

BRIGHTON, 7. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) RESIDENT PATHOLOGIST (Senior House Officer grade) required for Area Laboratory. Good experience in all branches of clinical pathology.

Applications, stating age, qualifications, experience and naming 2 referees, to the Administrative Officer.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) CASUALTY HOUSE SURGEON required 1st March. Duties include work in Orthopædic and Traumatic Unit. Recognised for pre-registration and F.R.C.S.

Applications, stating age, qualifications, &c., and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON to the Orthopædic Unit. Salary in accordance with national scales. This post is recognised as a pre-registration appointment. Vacant 12th February, 1958.

Applications, stating age, qualifications, and experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

BRISTOL (near). HAM GREEN HOSPITAL, Pill, near BRISTOL. Applications are invited for the post of RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER in the Chest Diseases wards of the above Hospital. The Hospital is fully equipped for modern treatment of pulmonary tuberculosis and other diseases of the chest, including regular major thoracic surgery. Opportunity also for work in the Bristol Chest Clinic. Appointment for 1 year, renewable. Post now vacant.

Applications, with testimonials and names of referees, to the Secretary, Ham Green Hospital, Pill, near Bristol.

BRISTOL. COSSHAM AND FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in Pathology required 1st April, 1958, at Frenchay Hospital (542 Beds—general medicine, general surgery and thoracic, neuro-surgical and plastic units for the South West.) Post may be resident or non-resident but residence essential when on call. It provides training in all branches of Clinical Pathology. Laboratory is recognised for Diploma in Pathology. Some duties in connection with the Regional Blood Transfusion Service.

Detailed applications, quoting 2 referees, to the Group Secretary, Frenchay Hospital, Bristol.

BROMSGROVE, WORCESTERSHIRE. HILL TOP HOSPITAL. (76 Beds.) REGIONAL THORACIC SURGICAL CENTRE. Applications are invited for the post of Locum HOUSE PHYSICIAN at the above Hospital.

Applications, with the names of 3 referees, to the Hospital Secretary, Bromsgrove General Hospital, Worcestershire.

BROMSGROVE, WORCESTERSHIRE. HILL TOP HOSPITAL. (76 Beds.) REGIONAL THORACIC SURGICAL CENTRE. Applications are invited for the post of Locum HOUSE SURGEON at the above Hospital.

Applications, with the names of 3 referees, to the Hospital Secretary, Bromsgrove General Hospital, Worcestershire.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEONS (3). Applications are invited for 3 pre-registration posts in General Surgery. Posts still vacant. 2 of the posts are at Bury General Hospital and the third at Rossendale General Hospital.

Apply, stating age, qualifications and other details, to the Group Secretary at Bury General Hospital, Bury, Lancs.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. House OFFICER to Departments of Dermatology, Ophthalmology and Pædiatrics for 6 months from April 17th. Recognised pre-registration service (medical) and for D.C.H. and D.O.

Apply, stating age, nationality, qualifications and experience, with dates, and copies of 3 testimonials, to the Secretary by 1st March. Interviews mid-March.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of GENERAL SURGICAL AND UROLOGICAL HOUSE SURGEON (pre-registration or third post), which is recognised for the F.R.C.S., is now vacant. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CARDIFF. THE UNITED CARDIFF HOSPITALS AND THE WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR in Urology. The appointment (vacant mid-March) is a joint one between the United Cardiff Hospitals and the Welsh Regional Hospital Board, the time divided equally between the 2 Boards.

Application forms are available from the Secretary to the Board of Governors, United Cardiff Hospitals, Cardiff Royal Infirmary, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CARLUKE, LANARKSHIRE. LAW HOSPITAL. (780 Beds.) Applications are invited for the undernoted posts:—

(*a*) JUNIOR HOSPITAL MEDICAL OFFICER and (*b*) HOUSE OFFICER in Orthopædic Surgery. The unit consists of 120 Beds and deals with acute orthopædic and accident work from a large part of Lanarkshire, and offers excellent experience.

(*c*) RESIDENT HOUSE SURGEON (pre- or post-registration) for the 6 months commencing 1st February, 1958.

(*d*) Locum ANÆSTHETIST (Senior House Officer or Junior Hospital Medical Officer grading) for a period of 2 months.

Applications, stating age, qualifications and previous experience, together with the names of 2 referees, should be sent to the Group Medical Superintendent, Law Hospital, Carluke, as soon as possible.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. (733 Beds.) SENIOR HOUSE OFFICER to the Obstetric and Gynæcological Department (75 obstetric and 60 gynæcological beds). Post vacant 14th April. Experience in obstetrics and gynæcology essential; post recognised for M.R.C.O.G. Appointment for 6 months with possibility of renewal for further 6 months.

Applications, stating age, qualifications and experience, with copies of recent testimonials and the names of 2 referees, should be sent to Group Secretary at above address, by 26th February.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON. Pre-registration post. The post offers good surgical experience. Recognised for the F.R.C.S.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) Locum GENERAL SURGICAL REGISTRAR required from 17th February to 9th March, 1958, inclusive.

Applications to Physician-Superintendent, St. Peter's Hospital, Chertsey, as soon as possible.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) RESIDENT HOUSE SURGEON (Senior House Officer or Intern) required for Gynæcological (30 Beds) and E.N.T. (approximately 14 Beds) Departments. Salary in accordance with terms and conditions of National Health Service. Post vacant April.

Applications, together with names and addresses of referees, to Physician-Superintendent, St. Peter's Hospital, as soon as possible.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) Locum CASUALTY OFFICER required (Senior House Officer grade) from 16th February, 1958, to 1st March, 1958, inclusive. Resident or non-resident.

Applications as soon as possible to Physician-Superintendent, St. Peter's Hospital, together with names and addresses of referees.

CHELTENHAM GENERAL HOSPITAL. (220 Beds.) HOUSE SURGEON required (pre- or post-registration). 1st March, 1958. The post offers a wide experience in general surgery, gynæcology, and orthopædic surgery. Post recognised for the F.R.C.S.

Applications, with names of 2 referees, to be sent to Secretary, General Hospital, Cheltenham.

CHELTENHAM MATERNITY HOSPITAL. Cheltenham GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of RESIDENT OBSTETRIC OFFICER. The Hospital, which is recognised for the purpose of training for the D.Obst.R.C.O.G., has 50 Beds and deals with the majority of abnormal midwifery cases in North East Gloucestershire. The appointment is for a period of 6 months and the salary will be £577 10s. less charge for residential emoluments. The appointment is vacant immediately.

Applications, stating age, qualifications and experience, and accompanied by copies of 3 recent testimonials, should be sent to the Secretary, Cheltenham Group Hospital Management Committee, General Hospital, Cheltenham.

CHICHESTER. ROYAL WEST SUSSEX HOSPITAL. (202 acute beds.) RESIDENT HOUSE SURGEON required for 6 months' appointment. National salary scales for either provisionally or fully registered practitioners. Post approved for pre-registration practitioners, and F.R.C.S. 8 residents. Vacant end of February.

Applications, stating age, experience, qualifications, with reference or names of referees, to Senior Administrative Officer.

COATBRIDGE, AIRDRIE AND DISTRICT HOSPITALS BOARD OF MANAGEMENT. JUNIOR HOSPITAL MEDICAL OFFICER required for Lightburn Infectious Diseases Hospital and Sanatorium, Shettleston, and Coathill Hospital, Coatbridge (infectious diseases and geriatric patients). Resident accommodation available. Salary scale £852 10s.–£1182 10s. p.a.

Applications, stating age, nationality and details of training, qualifications and experience, together with the names of 3 referees, should be lodged as soon as possible with the Group Secretary, Hairmyres Hospital, East Kilbride.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for :—

Essex County Hospital, Colchester (189 Beds)

Post of HOUSE SURGEON. Recognised for F.R.C.S.

First, second, third or pre-registration post, tenable for 6 months.

St. Mary's Hospital, Colchester

Post of SENIOR HOUSE OFFICER (Resident Medical Officer) for Geriatric Unit. Includes duties in connection with medical and surgical patients accommodated at hospital and duties at Essex County Hospital (general medical). Post tenable for 6 or 12 months. Resident.

Applications, with copies of 3 testimonials, to Secretary, Colchester Group Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

COULSDON, SURREY. CANE HILL HOSPITAL. Cane HILL HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Psychiatry, whole-time. Accommodation available if required for single man or woman. The Hospital has 5 outpatient clinics and undertakes postgraduate teaching in association with the Institute of Psychiatry. Every facility will be given for further study. Candidates may visit the hospital by arrangement with the Physician-Superintendent.

Application forms, returnable within 14 days, may be obtained from the Group Secretary.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH. RESIDENT JUNIOR HOUSE SURGEON (general surgery). Pre-registration post now vacant. Tenable 6 months. Health Service conditions.

Applications, stating age, nationality, qualifications and experience, with names of 2 referees, to Group Secretary, Mid-Sussex Hospital Management Committee.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH, SUSSEX. RESIDENT SENIOR HOUSE OFFICER (general surgery). Post vacant 24th February. Tenable 6 months in first instance.

Applications, stating age, qualifications, nationality and experience, with names of 2 referees, to Group Secretary, Mid-Sussex Hospital Management Committee.

DARLINGTON (near). AYCLIFFE HOSPITAL FOR MENTAL DEFECTIVES, HEIGHINGTON, near DARLINGTON, CO. DURHAM. Locum JUNIOR HOSPITAL MEDICAL OFFICER required for an approximate period of 6 weeks commencing on 10th March, 1958, at the above Hospital. Salary £19 5s. per week, less an amount of £3 5s. 2d. per week in respect of residential accommodation.

Applications to the Medical Superintendent.

T. H. ALLAN, Group Secretary.

DERBY CITY HOSPITAL. (Obstetrical Department—76 Beds.) DERBY NO. 1. HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of OBSTETRIC HOUSE SURGEON. Pre-registration or Senior House Officer. Vacant 1st April, 1958. This post is recognised in Obstetrics by the Royal College of Obstetricians and Gynæcologists—if held by Senior House Officer.

Applications, stating age, qualifications and experience, with copies of 2 testimonials, should be sent to the Medical Superintendent, City Hospital, Derby.

DONCASTER ROYAL INFIRMARY. (330 Beds. Recognised for the D.A. and F.F.A. R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required 1st April. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th February, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DONCASTER. WESTERN HOSPITAL. (Recognised under the regulations for the D.Obst.R.C.O.G. and M.R.C.O.G. (obstetrical experience) and approved for pre-registration service under the Medical Act, 1950.) Applications are invited for the post of OBSTETRICAL HOUSE OFFICER (Senior House Officer or pre-registration post). Vacant beginning March.

Applications should be forwarded to the Group Secretary, Doncaster Hospital Management Committee, at Doncaster Royal Infirmary by 18th February.

DENBIGH. THE NORTH WALES HOSPITAL FOR NERVOUS AND MENTAL DISORDERS. JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER required. The Hospital has modern treatment facilities, and is recognised by the Conjoint Board for the purpose of their D.P.M. examination. House available for married man and family.

Applications, with names of 2 referees, to the Medical Superintendent.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP, BIRMINGHAM REGION.

The Corbett Hospital, Stourbridge (114 Beds)

HOUSE OFFICER (surgical), pre-registration. Post vacant now.

Wordsley Hospital, near Stourbridge (478 Beds)

HOUSE OFFICER (surgical), pre-registration. Post vacant now.

Prestwood Sanatorium, near Stourbridge (199 Beds. Tuberculosis)

Locum JUNIOR HOSPITAL MEDICAL OFFICER, resident, required for a period of 1 year.

Apply Group Secretary, Guest Hospital, Dudley, Worcs.

DUDLEY. STOURBRIDGE GROUP. Registrar (anæsthetics). Post vacant 1st March. Experience specialty essential. Post recognised for F.F.A. R.C.S. Duties at Wordsley, Corbett and The Guest Hospitals. Opportunity for experience in general surgery, gynæcology, orthopædics, and plastic surgery with the Regional Plastic Surgery Unit. Resident at Wordsley Hospital. Married accommodation available.

Application forms from Group Secretary, Guest Hospital, Dudley, to be returned by 24th February, 1958. Candidates may visit hospitals.

DURHAM. COUNTY HOSPITAL. (116 Beds.) Senior HOUSE OFFICER in Orthopædics required immediately. Resident. The County Hospital is the main Orthopædic and Accident Hospital in a busy mining and industrial area. Experience can be obtained in all branches of orthopædics.

Applications, with particulars of previous experience and names of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

DURHAM. COUNTY HOSPITAL. (116 Beds.) Resident HOUSE SURGEON required in Orthopædics and Casualty. Post recognised for pre-registration purposes. This post offers facilities for good and varied experience in a busy orthopædic and accident hospital which serves a wide mining and industrial area.

Apply, giving age, experience and names of 2 referees, to the Group Secretary, Dryburn Hospital, Durham.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR, County Hospital, Doddington, Cambridgeshire. (116 Beds.) Post provides good experience in general and orthopædic surgery. Self-contained flat available. Appointment for 1 year renewable for second year.

Applications, stating age, experience and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 3rd March, 1958. Candidates invited to visit hospital by direct arrangement with the Surgeon-Superintendent.

EDINBURGH. CHALMERS HOSPITAL. Applications are invited from registered or pre-registration medical practitioners for appointment of RESIDENT HOUSE SURGEON in the Gynæcological Annexe of the above Hospital, for 6 months commencing 1st April, 1958 (a training post for R.C.O.G. membership).

Applications, stating age, qualifications and experience, and names of 2 referees, to be sent immediately to the Secretary, Edinburgh Central Hospitals, 1, Rillbank-terrace, Edinburgh.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. RESIDENT HOUSE SURGEON, pre-registration post. Vacant 3rd March, 1958. Duties with general surgical unit, doing some genito-urinary work. Post recognised by the Royal College of Surgeons. 6 months' appointment.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital.

EPPING. ST. MARGARET'S HOSPITAL. Resident SENIOR HOUSE OFFICER (obstetrics), vacancy occurring 1st April. Post recognised for D.Obst.R.C.O.G. Busy general hospital with easy access to London.

Applications, with 2 recent testimonials, to the Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage," The Plain, Epping, Essex, by 21st February, 1958.

GLOUCESTER. HORTON ROAD AND CONEY HILL HOSPITALS. (1540 Beds.) Applications invited for the appointment of a JUNIOR HOSPITAL MEDICAL OFFICER. Hospitals serve the North Gloucestershire Clinical Area, including Gloucester, Cheltenham, Stroud, and Forest of Dean. High admission-rate (850). All modern methods of treatment. New units provide for treatment of neurosis and alcoholism. Expanding outpatient services, day-hospital, long-stay annexes and social clubs. Encouragement and opportunity for study. Salary and conditions Whitley Council. Single accommodation available.

Applications, with names of 3 referees, to Physician-Superintendent.

HEXHAM GENERAL HOSPITAL. (304 Beds.) Junior HOSPITAL MEDICAL OFFICER (surgery). Hospital recognised by Royal College of Surgeons.

Applications, with names of 2 referees, as early as possible to Group Secretary, General Hospital, Hexham, Northumberland.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL (150 Beds.) Applications are invited for the post of CASUALTY AND ORTHOPÆDIC HOUSE SURGEON, 1 of 2 similar posts graded Senior House Officer. Post vacant 22nd February, 1958.

Apply, with 2 testimonials or the names of 2 referees, to the Hospital Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Applications are invited for the post of HOUSE SURGEON (surgery/E.N.T.—pre-registration), vacant on 20th February, 1958. This Hospital is the main surgical hospital in the Hastings area and the post offers excellent experience.

Apply, with 2 testimonials or the names of 2 referees, to Hospital Administrator.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. RESIDENT SENIOR HOUSE OFFICER, for duty with Accident Service, and care of Traumatic and Orthopædic Inpatients, required 17th March, 1958. Post recognised for F.R.C.S.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to the Medical Administrator, Lister Hospital.

HOUNSLOW HOSPITAL. (General acute—81 Beds.) Applications are invited for the appointment of RESIDENT CASUALTY OFFICER (Senior House Officer grade), recognised for F.R.C.S. examination. Post vacant 1st March, 1958. Salary £819 10s. less £150 p.a. for residence, &c.

Applications, stating age, qualifications, experience, with copies of 3 recent testimonials or names for reference, to the Hospital Secretary, Hounslow Hospital, Staines-road, Hounslow, Middlesex.

HOVE GENERAL HOSPITAL. Senior House Officer (recognised for F.R.C.S.) required on 17th April, 1958. Duties of Resident Surgical Officer. Appointment for 1 year.

Applications, stating age, qualifications and full details of experience, together with names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Sackville-road, Hove, 3.

HOVE GENERAL HOSPITAL. Pre-registration House SURGEON (with ward and casualty duties) required for a period of 6 months from 10th March, 1958. This post is recognised for the F.R.C.S. and provides a wide experience in an active surgical unit.

Applications, stating age, qualifications, and full details of experience, together with the names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Sackville-road, Hove, 3.

HOVE GENERAL HOSPITAL. Pre-registration House PHYSICIAN required on 18th March, 1958, for a period of 6 months. Excellent clinical material available. Post is suitable for candidate working for a higher degree.

Applications, stating age, qualifications, and full details of experience, together with names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Sackville-road, Hove, 3.

HUNTINGDON COUNTY HOSPITAL. Applications are invited for the post of HOUSE OFFICER (surgical) now vacant. Post recognised for pre-registration purposes.

Apply, with full particulars and names of 2 referees, to Secretary, County Hospital, Huntingdon.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from provisionally registered medical practitioners for the post of HOUSE PHYSICIAN, to commence duties on 1st March, 1958. Salary in accordance with national scales.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. HOUSE SURGEON required immediately. Recognised for D.C.H. An interesting and varied post which includes outpatient and casualty work.

Applications, together with details of experience, testimonials, &c., to the Hospital Secretary.

ILFORD. KING GEORGE HOSPITAL. (General hospital—211 Beds.) There is a vacancy for a SENIOR HOUSE OFFICER, Orthopædic Department at above Hospital. Salary will be at the rate of £819 10s. p.a., less emoluments. Recognised for the F.R.C.S.

Applicants should have been registered not less than 1 year and should send applications, accompanied by copies of 3 testimonials to the undersigned, within 7 days of the appearance of this advertisement.

H. F. HARRIS, Group Secretary, Ilford and
Barking Group Hospital Management Committee.

King George Hospital, Ilford.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in General Medicine, vacant early March. The post offers excellent experience and opportunity for working for higher qualifications (M.R.C.P.). There are approximately 50 acute medical beds.

Applications, stating age, nationality and previous experience, together with copies of recent testimonials, to Hospital Secretary by 24th February, 1958.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the E.N.T. and Ophthalmic Departments. The post is recognised for pre-registration and for the D.L.O. examination.

Applications, giving full particulars and copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the Fracture and Orthopædic Department. Approved pre-registration post.

Applications, with copies of recent testimonials, to the Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Heath-ROAD WING), IPSWICH. Pre-registration post of HOUSE SURGEON to General Surgeon vacant. Recognised for R.C.S. examination.

Applications, with copies of recent testimonials, to Hospital Secretary.

ILKLEY. MIDDLETON HOSPITAL. (430 Beds.) Resident SENIOR HOUSE OFFICER (surgical) required for Major Thoracic Surgical Unit at the above Hospital.

Applications, stating age, nationality, qualifications and experience, to Hospital Secretary.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR (non-resident except on duty nights), vacant immediately. Higher qualification desirable. Recognised for F.F.A. R.C.S. Department comprises 3 teams, and every kind of surgical work is carried out except thoracic and neurosurgery. Post includes work at neighbouring hospitals.

Application forms obtainable from and returnable to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 25th February.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. Senior HOUSE OFFICER, Department of Orthopædics and Traumatic Surgery (58 Beds). Vacant March. Post tenable for 6–12 months. Offers useful surgical experience. Recognised for F.R.C.S.

Applications, stating age, qualifications, medical experience, and copies of up to 2 testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 25th February.

KEIGHLEY AND DISTRICT VICTORIA HOSPITAL, KEIGHLEY, YORKSHIRE. (General—139 Beds.) RESIDENT HOUSE PHYSICIAN required immediately for period of 4 months or for full term of 6 months. Approved pre-registration appointment. 4 residents on staff.

Applications, with full particulars as to age, nationality and qualifications, and copies of 2 testimonials, to be sent to Group Secretary, Hospital Management Committee, 17, St. John's Hospital, Keighley, as soon as possible.

KETTERING AND DISTRICT GENERAL HOSPITAL, NORTHAMPTONSHIRE. Applications are invited for the post of HOUSE SURGEON (pre-registration), vacant 1st February, 1958. Post recognised for F.R.C.S.

Applications, stating age, experience, and qualifications, together with copies of 3 recent testimonials, to be sent to the Group Secretary at the above address.

KETTERING AND DISTRICT GENERAL HOSPITAL. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. The post, vacant now, offers wide experience of all traumatic conditions including fractures and some orthopædic cases with charge of 30 Beds.

Applications, accompanied by testimonials, to be sent to the Group Secretary, General Hospital, Kettering.

LANCASTER. ROYAL LANCASTER INFIRMARY. (240 Beds.) SENIOR HOUSE OFFICER (casualty). The successful applicant will work with the specialist orthopædic unit. The post is recognised for F.R.C.S.

Applications, with names of 2 referees, to be addressed to the Group Secretary, Royal Lancaster Infirmary, Lancaster.

LANCASTER. ROYAL LANCASTER INFIRMARY. (240 Beds.) RESIDENT HOUSE OFFICER (surgical) (pre-registration post). Successful applicant will work with Consultant Surgical Unit and attend Consultative Clinics. Post tenable for 6 months. Recognised for F.R.C.S.

Applications, with names of 2 referees, to the Secretary, Royal Lancaster Infirmary, Lancaster.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Anæsthetics

Leeds A and B Groups. Recognised for F.F.A. R.C.S. and D.A. Resident.

Thoracic Surgery

Regional Thoracic Centre, Pinderfields General Hospital, Wakefield (56 Beds). Recognised for F.R.C.S. Accommodation for a single person.

Psychiatry

(i) Oulton Hall Hospital, near Wakefield, and Affiliated Mental Deficiency Colonies. (Approximately 400 Beds.) Non-resident.

(ii) Storthes Hall Hospital, Huddersfield (2750 Beds).

If desired, facilities for attendance at the Leeds University will be provided, if the successful candidates are studying for the D.P.M.

Rheumatism Research

The Leeds Regional Hospital Board in association with The University of Leeds invites applications for the post of RESEARCH REGISTRAR in Rheumatism to assist the Professor of Clinical Medicine with research projects at the Royal Bath Hospital, Harrogate, which is the centre for the Regional Rheumatism Scheme, or elsewhere in the Region.

Applications, stating age, sex, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 19th February, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Senior Registrars in Psychiatry for duties at:—

(i) Storthes Hall Hospital, Kirkburton, near Huddersfield (2600 Beds), and associated clinics. Duties will also include visits to the Neurological and E.E.G. Unit at the General Infirmary at Leeds. Resident or non-resident.

(ii) De la Pole Hospital, Willerby, Hull (1000 Beds). This hospital has a high admission-rate and a separate neurosis unit for females. Duties also include visits to the Psychiatric Day Centre, Hull, and an outpatient clinic at Goole. Small flat available for married person, otherwise non-resident.

Successful candidates for both appointments will undertake 2 clinical sessions (which may include research) in association with the Department of Psychiatry of the University of Leeds. Candidates for both these appointments should hold the D.P.M. or equivalent qualification.

Applications, stating age, qualifications and details of appointments held showing dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 5th March, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Anæsthetics

Duties in the Hull A, B, and East Riding Groups. Recognised for the F.F.A. R.C.S. Duties may include thoracic anæsthesia. Non-resident.

Chest Diseases

Duties at Castle Hill Sanatorium, Cottingham, East Yorkshire (220 Beds). Resident.

General Medicine

Duties at Halifax General Hospital (110 general medical beds). Resident.

General Surgery

Duties at Pinderfields General Hospital (70 general surgical beds). Post involves duties of Resident Surgical Officer. Recognised for F.R.C.S. Accommodation available for a single person.

Applications, stating age, qualifications and details of present and previous appointments, with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 26th February, 1958.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. Applications are invited for the post of REGISTRAR in Surgical Pathology to work in the Infirmary pathological service under the immediate direction of the Professor of Pathology. He will assist on a full-time basis in the routine surgical biopsy diagnostic service (4000 biopsies annually) and will be responsible for the running of the Registry of Cases (follow-up). Opportunity will be afforded for some ward and clinic attendance and for research in the field of surgical pathology. The post, which is non-resident, will be for 1 year in the first instance but is renewable.

Applications, stating age, qualifications, experience and professional objectives and with the names of 3 referees, should be sent to the Sub-Dean, School of Medicine, Leeds, 2, from whom further particulars may be obtained in writing. Closing date 8th March.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER in E.N.T. Department required for a period of 6 months. Post vacant now. Terms and conditions of service for hospital medical staffs apply.

Applications, giving details of age, qualifications, posts held with dates, and 3 names for reference, should be sent to the Secretary to the Board, as soon as possible.

LEEDS. UNITED LEEDS HOSPITALS/LEEDS REGIONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR in Psychiatry associated with the Leeds University Department of Psychiatry. The successful candidate will undertake duties in connection with the clinical, teaching and research work of the Department at the General Infirmary and St. James's Hospital, Leeds. Candidates should hold high medical qualifications and a Diploma in Psychological Medicine or equivalent.

Applications, stating age, qualifications and details of appointments held, showing dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 5th March, 1958.

LEWES (near). CHAILEY HERITAGE (Craft School and Hospital), NORTH CHAILEY, near LEWES, SUSSEX (300-Bedded children's orthopædic hospital). MID-SUSSEX HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER. Resident post now vacant, tenable 3 years initially. Work covers long-term orthopædics and pædiatric conditions. Previous experience as either Orthopædic House Surgeon or Pædiatric House Physician necessary. Interested candidates invited to visit.

Apply, with names of 2 referees, to Medical Administrator.

LINCOLN COUNTY HOSPITAL, Sewell-road, Lincoln. (200 Beds.) Applications are invited for the appointment of RESIDENT HOUSE SURGEON (Male or Female). This is an approved pre-registration post which becomes vacant in February, 1958. The duties are with a general surgeon. This post will be followed, if satisfactory, by appointment for a further 6 months as House Physician.

Applications, with copy testimonials, should be sent to the Group Secretary, Lincoln County Hospital, as soon as possible.

LINCOLN. ST. GEORGE'S HOSPITAL. (242 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR/SENIOR HOUSE OFFICER (pædiatrics) required. Duties include care of new-born and premature babies, exchange transfusions, neonatal surgery and duties at a maternity unit at Lincoln County Hospital. This post offers excellent opportunity for the study of metabolic diseases in childhood and infancy. A new cubicled unit is being opened. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th February, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LINCOLN. HARMSTON HALL HOSPITAL. Junior HOSPITAL MEDICAL OFFICER (resident) required for group of mental deficiency hospitals in Lincolnshire (943 Beds). Salary scale £852 10s.–£55–£1182 10s., with national terms and conditions of service. Car required, travelling expenses according to scale.

Applications, with full details of age, education, qualifications, previous appointments with dates, and 2 names for reference, to be sent to Group Secretary, Harmston Hall, Lincoln, within 10 days.

LEICESTER GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics), vacant 1st April. Recognised for the D.C.H.

Applications, stating age, qualifications and experience, together with copies of recent testimonials, to the Group Secretary, Leicester No. 1 Hospital Management Committee, The Leicester Royal Infirmary, forthwith.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for temporary appointment to the post of SENIOR HOUSE OFFICER (resident) in Gynæcology for duty at the Women's Hospital for the period from 1st April (or as soon as possible thereafter) to the 30th September, 1958.

Apply by 1st March, 1958, on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for the following House Officer posts for the 6 months beginning 1st March, 1958.

David Lewis Northern Hospital

HOUSE SURGEON (orthopædic).

CASUALTY OFFICER.

Liverpool Stanley Hospital

HOUSE SURGEON (orthopædic and casualty).

The posts are open to registered and pre-registration applicants.

Apply as soon as possible on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL, 20. BOOTLE HOSPITAL. There is a vacancy for HOUSE SURGEON to start as soon as possible. Recognised for pre-registration service.

Apply to Secretary, Walton Hospital, Liverpool, 9.

LLANELLY HOSPITAL, Llanelly, Carmarthenshire. (162 Beds.) GLANTAWE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER in the Gynæcological Department, with duties in the E.N.T. and Ophthalmic Departments.

Full particulars, stating age, qualifications and experience, should be addressed to the Hospital Secretary.

LLANELLY HOSPITAL, Llanelly. (162 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of HOUSE OFFICER in the Medical Unit of the above Hospital. The post is recognised for pre-registration purposes. Immediate vacancy.

Applications, with full particulars, should be sent to the Secretary of the Hospital. T. E. JONES, Group Secretary.

LLANELLY HOSPITAL, Llanelly. (162 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of HOUSE OFFICER in the Surgical Unit of the above Hospital. The post is recognised for pre-registration purposes. Immediate vacancy.

Applications, with full particulars, should be sent to the Secretary of the Hospital. T. E. JONES, Group Secretary.

LUTON AND DUNSTABLE HOSPITAL, Luton, BEDFORDSHIRE. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR (resident) required at the above Hospital. Post vacant 1st April, 1958. The Hospital may be visited by direct appointment.

Application forms obtainable from Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton, Beds, and should be returned by 21st February, 1958.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedfordshire. HOUSE SURGEON, post now vacant. Tenable for 6 months. Recognised as pre-registration post and for F.R.C.S.

Applications stating age, nationality, qualifications and experience, together with copies of two recent testimonials, to the Secretary of the Hospital.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months' appointment. Post vacant immediately. Salary at the rate of £467 10s.–£577 10s. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

MANCHESTER REGIONAL HOSPITAL BOARD. Salford HOSPITAL MANAGEMENT COMMITTEE. HOPE HOSPITAL, SALFORD, 6. ORTHOPÆDIC REGISTRAR required, 60 adult and children's beds. Duties also at Salford Royal and Royal Manchester Children's Hospitals. Post recognised for F.R.C.S., and there is also a share of emergency general surgery with 2 general surgical registrars.

Applications to Group Secretary, Salford Royal Hospital, Salford, 3, before 1st March, 1958.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of REGISTRAR in Thoracic Surgery to the Blackpool and Fylde Group of hospitals with main duties at the Victoria Hospital, Blackpool. The post, immediately available, is recognised for the F.R.C.S. and offers a sound experience gained with the 2 Consultant Thoracic Surgeons who are responsible for the thoracic surgery in the Northern part of the Manchester Region. Non-resident post but residential accommodation is available if required for single applicants.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Group Secretary, Victoria Hospital, Blackpool.

MANCHESTER REGIONAL HOSPITAL BOARD. Whole-time MEDICAL OFFICER (Junior Hospital Medical Officer, tenable for 4 years), Regional Blood Transfusion Service, Roby-street, Manchester, to assist in the laboratory and at bleeding sessions. Previous experience of this work desirable. Appointee will work under direction of the Consultant and Director of the Service and opportunities for research are available.

Applications, with names, &c., of 2 referees, to be forwarded to the Senior Administrative Medical Officer of the Board at Cheetwood-road, Manchester, 8, by 3rd March, 1958.

MIDDLESBROUGH. HEMLINGTON HOSPITAL. (282 Beds.) TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE SURGEON. This post offers experience in connection with acute surgery, gynæcology and plastic surgery beds.

Applications, stating age, qualifications and names for reference, to be forwarded to the Hospital Secretary.

NEWBURY DISTRICT HOSPITAL, Newbury, Berkshire. (90 Beds.) READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of RESIDENT SENIOR HOUSE OFFICER (general surgery); married quarters available.

Write, stating age, qualifications with dates, nationality and present post, together with the names of 3 referees, to Group Secretary, Reading and District Hospital Management Committee, 3, Craven-road, Reading.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the non-resident appointment of SENIOR HOUSE OFFICER in the Throat, Nose and Ear Department at the Royal Victoria Infirmary. The appointment is for 1 year in the first instance and is subject to the terms and conditions of service of medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER in the Department of Obstetrics and Gynæcology. The successful candidate will have duties in the Royal Victoria Infirmary (resident or non-resident) and the Princess Mary Maternity Hospital (resident). The appointment is recognised for examination purposes by the Royal College of Obstetricians and Gynæcologists. The appointment is for 1 year and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service. The salary will be at the rate of £819 10s. p.a., subject to the appropriate deductions.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE REGIONAL HOSPITAL BOARD. REGISTRAR PSYCHIATRIST, whole-time at Newcastle General Hospital, Department of Psychological Medicine (54 Beds). This department is associated with the University of Durham and is under the direction of the Professor of Psychological Medicine. It is the principal postgraduate teaching and research unit in the Region. The person appointed will be able to take the course for the Durham D.P.M. Training will be given in all aspects of psychological medicine including child psychiatry and mental deficiency. Further particulars from Regional Psychiatrist.

Applications, together with names and addresses of 3 referees, to the Regional Psychiatrist, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWPORT, I.W. ST. MARY'S HOSPITAL. (350 Beds.) SENIOR HOUSE OFFICER required as Casualty Officer (recognised for F.R.C.S.) and as House Officer to Consultant Obstetrician and Gynæcologist. Vacant April. Salary £819 10s., less residential charge. Modern flat available for married candidate.

Applications, with names of 2 referees, to Hospital Secretary not later than 1st March.

NORWICH. ST. ANDREW'S HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER (Male) for duty at the Mental Hospital of 240 Beds at Great Yarmouth which is to be attached to the St. Andrew's Group as from 1st April, 1958. Accommodation available for a single or married man. National Health Service salaries and conditions apply. Previous experience in psychiatry desirable but not essential.

Further particulars may be obtained from the Medical Superintendent, St. Andrew's Hospital, Thorpe, Norwich, to whom applications, giving details of age, qualifications, experience, and the names of 2 referees, should be addressed as soon as possible.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty), duties to commence about 14th February. Establishment 3. Recognised for F.R.C.S. Post offers wide experience of casualty work.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Secretary, General Hospital, Nottingham.

NOTTINGHAM. HIGHBURY HOSPITAL, Bulwell, NOTTINGHAM. Locum SENIOR HOUSE OFFICER (resident) required for obstetrical and medical duties for period 17th March–17th April, 1958.

Apply, stating qualifications and experience, to the Hospital Secretary.

NOTTINGHAM CITY HOSPITAL. (611 Beds.) Applications are invited for the post of HOUSE SURGEON, vacant 15th February, 1958. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM CITY HOSPITAL. (611 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer), vacant 6th April, 1958. The post is recognised for the D.A. and the F.F.A. R.C.S. and offers wide experience. This is a busy general hospital with Departments in General, Orthopædic, Gynæcological, Thoracic and Plastic Surgery.

Applications, stating age, nationality and qualifications, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM. HEATHFIELD HOSPITAL, Hucknall-road, NOTTINGHAM. (Infectious diseases.) Resident Locum MEDICAL OFFICER (Male or Female) required immediately for holiday period of 3–4 weeks. Junior Hospital Medical Officer rate of £19 5s. per week, less residential emoluments. Previous fever experience not essential.

Applications, with copies of 2 recent testimonials, as soon as possible to Physician-Superintendent.

ORPINGTON HOSPITAL, Orpington, Kent. Resident SENIOR HOUSE PHYSICIAN (Male or Female) for Geriatric Department. Post offers good clinical experience and opportunity for higher studies. Hospital may be visited by appointment.

Applications, with copies of 2 recent testimonials, to Surgeon-Superintendent.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEONS required for General Surgical Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEON required for Orthopædic Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, FREEDOM FIELDS. Central Casualty Department. RESIDENT SENIOR HOUSE OFFICER in Casualty vacancies, 1 immediately, and 1st April, 1958. Recognised for the F.R.C.S.

Applications, stating names of 3 referees, to be sent to the Group Secretary.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

(1) **Saint Mary's Hospital**
HOUSE SURGEON (pre-registration). Vacant now and 11th February, 1958.

(2) **Royal Portsmouth Hospital**
HOUSE SURGEON (pre-registration). Vacant 14th March 1958.

(3) **Queen Alexandra Hospital**
HOUSE SURGEON (pre-registration). Vacant 12th February, 1958.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

READING AREA DEPARTMENT OF MEDICINE. READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered and provisionally registered medical practitioners for 2 posts as RESIDENT HOUSE PHYSICIAN, vacant 1st March, 1958, for a period of 6 months. Successful candidates will be required to carry out duties at the following Reading hospitals: Royal Berkshire Hospital (397 Beds), Battle (374 Beds), and Prospect Park (104 Beds).

Write immediately, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

READING. BATTLE HOSPITAL. (391 Beds.) **Reading** AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON in the Accident and Orthopædic Department. F.R.C.S. recognised. Also casualty duties.

Apply, stating age, qualifications with dates, nationality, present post, with copy of recent testimonial, to Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. (397 Beds.) READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered and provisionally registered medical practitioners for the resident post of HOUSE SURGEON, vacant 1st March, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. (397 Beds.) READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered and provisionally registered medical practitioners for the resident post of HOUSE PHYSICIAN in the Pædiatric Department, vacant 1st March, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary.

RICHMOND, SURREY. ROYAL HOSPITAL. (General hospital—121 Beds.) CASUALTY OFFICER required 18th March. Non-resident Senior House Officer grade. Recognition for F.R.C.S. being sought.

Apply, giving full particulars, including names of 2 referees, to Administrative Officer.

RICHMOND, SURREY. ROYAL HOSPITAL. Senior HOUSE SURGEON (resident) required immediately, for busy general hospital of 121 Beds with full consultant staff.

Apply, giving age, qualifications, experience and names of 2 referees, to Administrative Officer, immediately.

ROCHFORD GENERAL HOSPITAL. Locum Geriatric REGISTRAR required for period 3rd to 16th March, 1958, inclusive.

Applications to the Secretary at the above Hospital as soon as possible.

RHYL. ROYAL ALEXANDRA HOSPITAL. (138 Beds.) Applications are invited from registered medical practitioners for the post of HOUSE PHYSICIAN for the Departments of Medicine and Pædiatrics at the above Hospital. Post vacant 1st May, 1958.

Applications, stating age and experience, with copies of 2 testimonials, to be sent to the Group Secretary, Clwyd and Deeside Hospital Management Committee, "Rhianfa," Russell-road, Rhyl.

RHYL. ROYAL ALEXANDRA HOSPITAL. (138 Beds.) Applications are invited for the appointment of a CASUALTY OFFICER (Senior House Officer grade) at the above Hospital. Post recognised for F.R.C.S. Successful applicant will be required to commence duties 1st March, 1958.

Applications, stating age, qualifications, experience and nationality, accompanied by copies of 2 recent testimonials, should be sent to the Group Secretary, Clwyd and Deeside Hospital Management Committee, "Rhianfa," Russell-road, Rhyl.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) RESIDENT HOUSE SURGEON required immediately in the General Surgical Unit. Recognised for F.R.C.S. Open to either pre-registration applicants or to fully registered practitioners. This very active Unit of a total of approximately 180 Beds affords ample opportunities for candidates to obtain first-class tuition and experience. The candidates appointed will be attached to a unit of approximately 60 Beds.

Applications should be forwarded to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) RESIDENT HOUSE PHYSICIANS (2) required from 23rd February and 1st March, 1958, respectively. Open to either pre-registration applicants or to fully registered practitioners.

Apply immediately to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital.

SALISBURY GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE SURGEON/HOUSE PHYSICIAN to run consecutively in this order for a period of 6 months in each post from 19th February, 1958. Post open to pre-registration candidates.

Apply, naming 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. DUNDEE AND ANGUS AREA. Geriatrics. Applications are invited for the post of SENIOR REGISTRAR in the Geriatric Service for Dundee and Angus. The post is based at Maryfield Hospital, Dundee, a general teaching hospital of 370 Beds associated with the University of St. Andrews. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 1st March, 1958.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Obstetrics and Gynæcology. Dundee Teaching Hospitals. Applications are invited for the post of RESIDENT REGISTRAR in Obstetrics and Gynæcology at Dundee Royal Infirmary (557 Beds) and Maryfield Hospital (370 Beds), the main general teaching hospitals associated with the University of St. Andrews. The post is recognised for M.R.C.O.G. Applicants should have held house appointments in obstetrics and gynæcology and have had experience in general medicine and surgery. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 1st March, 1958.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited from Women practitioners for the appointment of REGISTRAR in Obstetrics and Gynæcology at the Bruntsfield and Elsie Inglis Hospitals, Edinburgh, vacant on 1st April, 1958. The successful applicant may be required to reside in the Elsie Inglis Hospital.

Apply, giving particulars of age, qualifications and previous experience and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 8th March, 1958.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited from Women practitioners for the appointment of REGISTRAR in Surgery at Bruntsfield Hospital, Edinburgh.

Apply, giving particulars of age, qualifications and previous experience, and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 8th March, 1958.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance:—

REGISTRAR in E.N.T. Surgery for duties on a rotational basis at the Western Infirmary and the Ear, Nose and Throat Hospital, Glasgow.

REGISTRAR in Medicine based at the Medical Unit, Gartloch Hospital, Gartcosh, Glasgow.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 1st March, 1958.

SHEFFIELD, 5. CITY GENERAL HOSPITAL. Locum SENIOR HOUSE OFFICER (orthopædics) required for the period up to 14th July, 1958. Rate of pay £15 19s. per week.

Apply, giving full details, to the Group Secretary, Sheffield No. 1 Hospital Management Committee, Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the post of REGISTRAR in Clinical Pathology. Post vacant 1st May. The successful candidate may be required to work in any of the laboratories of the United Sheffield Hospitals.

Applications, with the names of 3 referees, should be sent not later than 22nd February to the Chief Administrative Officer, United Sheffield Hospitals, West-street, Sheffield, 1.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. SENIOR HOUSE OFFICER in Psychiatry required to work under the Professor of Psychiatry in the newly established Psychiatric Department.

Applications, stating age, qualifications and experience, with the names of 3 referees or copy testimonials, should be sent not later than 4th March, 1958, to the Superintendent, Royal Infirmary, Sheffield, 6.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT SENIOR REGISTRAR (psychiatry) required for duties at the Towers Hospital, Leicester, and Children's Psychiatric Clinics in Leicester and Leicestershire. Possession of a higher qualification desirable. Appointment for 1 year in first instance reviewable annually.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 3rd March, 1958.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. (120 acute surgical and 50 orthopædic beds.) CASUALTY OFFICER (Senior House Officer). Post recognised for Casualty by R.C.S. Duties in casualty and orthopædic departments. Non-resident (single accommodation available).

Applications to Secretary, Southlands Hospital.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

SHREWSBURY. ROYAL SALOP INFIRMARY. Ortho-PÆDIC/ACCIDENT HOUSE SURGEON (Senior House Officer). Successful applicant will be allowed to attend for 2 days a month at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry, for postgraduate study, with the Consultant. Post recognised under revised Fellowship regulations in respect of 6 months' training required for the final Fellowship examination. Vacant 1st March, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SOUTHAMPTON CHEST HOSPITAL. South West METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required for Thoracic Surgical Unit at above Hospital. Previous experience in general surgery as a Registrar essential. Possession of F.R.C.S. would be desirable. The Unit consists of 78 surgical beds and has a very active Cardiac Department.

Application forms may be obtained from the undersigned, to whom they should be returned not later than Wednesday, 26th February, 1958.

FRANK JENNINGS, Group Secretary,
Southampton Group Hospital Management Committee.
Bullar-street, Southampton.

SOUTHAMPTON CHEST HOSPITAL. (252 Beds.) SENIOR HOUSE OFFICER required, to be responsible for Infectious Diseases Unit. The duties are such as to suit a candidate reading for higher examinations. The Unit is sited at a Hospital possessing up-to-date tuberculosis and thoracic surgical units, whilst the Southampton Group of hospitals as a whole affords excellent opportunities for study and experience in all branches of medicine.

Applications, together with copies of recent testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds. Recognised for F.R.C.S.) ORTHOPÆDIC HOUSE SURGEON (post recognised for pre-registration service and tenable for 6 months). The Hospital is the centre to which all trauma from a large industrial town and port is directed, thus providing excellent experience in the treatment of traumatic conditions; patients with orthopædic conditions are drawn from a wide area.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) RESIDENT HOUSE SURGEON required. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) RESIDENT HOUSE PHYSICIAN required. Pre-registration candidates eligible.

Applications, with copies of testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton, as soon as possible.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (274 Beds) and **SOUTHAMPTON GENERAL HOSPITAL** (471 Beds). SENIOR HOUSE OFFICER (E.N.T.) required in February. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing hearing-aid centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) Locum Tenens ANÆSTHETIC REGISTRAR, resident, required from 1st to 28th March, 1958, inclusive. Post recognised for F.F.A. R.C.S. and D.A.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL. (384 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time GYNÆCOLOGICAL AND OBSTETRIC REGISTRAR required. Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, Herts, by 1st March, 1958.

ST. ALBANS (near), HERTFORDSHIRE. SHENLEY HOSPITAL (2356 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER. Unfurnished house available. Post offers experience in all branches of psychiatry, including modern forms of treatment. Previous experience in psychiatry essential. The Hospital is 15 miles from London, and may be visited by appointment.

Application forms obtainable from and returnable to the Group Secretary by 1st March, 1958.

SOUTHEND. GENERAL HOSPITAL. Applications are invited from registered or provisionally registered practitioners for the post of RESIDENT HOUSE SURGEON, vacant 9th March, 1958.

Applications, stating age, qualifications, &c. (1 testimonial sufficient from pre-registration candidates seeking first appointment), to reach the Secretary not later than 15th February, 1958.

SOUTHEND-ON-SEA HOSPITAL. Applications are invited for the appointment of RESIDENT ANÆSTHETIST (Senior House Officer grade). Post vacant 1st April, 1958. The appointment is recognised as fulfilling the conditions of the F.F.A. R.C.S. and the D.A.

Applications, stating age, experience and qualifications, with copies of 2 testimonials, should be sent to the Secretary at the General Hospital, Southend, not later than 20th February, 1958.

STOCKPORT INFIRMARY. (163 Beds.) Applications are invited for the post of HOUSE OFFICER (general surgery), which is approved for pre-registration purposes. Recognised for the F.R.C.S., vacant early March.

Applications, with copies of 2 testimonials, to the Group Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOCKTON AND THORNABY HOSPITAL, Stockton-ON-TEES. (130 Beds.) TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of Locum SENIOR HOUSE OFFICER (casualty) at the above Hospital, which post is now vacant.

Applications, with full details, should be addressed to the Hospital Secretary as soon as possible.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. HOUSE OFFICER (obstetrics and gynæcology) required, vacant shortly. Pre-registration post. Recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Applications to Hospital Secretary as soon as possible.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (815 Beds.) HOUSE OFFICER (general surgery) required, vacant mid-March. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to the Secretary at the Hospital.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. SENIOR HOUSE OFFICER (pædiatrics) required. Post vacant 1st April. Recognised D.C.H.

Applications, with copy testimonials, to the Secretary at the Hospital, as soon as possible.

SURBITON GENERAL HOSPITAL. (72 Beds.) Kingston GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE SURGEON (resident), which becomes vacant as at 1st April, 1958. Salary £819 10s. p.a., subject to a deduction at the rate of £150 p.a. in respect of board, lodging and other services. Appointment, suitable reading for higher qualification, will in the first instance be for a period of 6 months. Successful candidate will work direct with visiting Consultants and will be responsible for ward cases.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to the Administrative Officer, Surbiton General Hospital, Ewell-road, Surbiton.

SWINDON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for the appointment of SENIOR HOUSE OFFICER as Casualty Officer and Orthopædic House Surgeon at Great Western Hospital, Swindon. Post recognised by R.C.S. for 6 months of year's training under Fellowship regulations. Work of Accident and Orthopædic Department, associated with Nuffield Orthopædic Centre (Wingfield Morris Orthopædic Hospital), Oxford, includes large number of industrial injuries. Salary £819 10s. p.a., less charge for residential emoluments.

Full details and names of 3 referees to Secretary, 7, Okus-road, Swindon, Wiltshire, immediately.

TALGARTH, BRECON. MID-WALES HOSPITAL. WELSH BORDER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Mental Hospital. Resident. A 4-roomed flat is available. The Hospital is recognised for Conjoint D.P.M.

Further particulars from and applications to Medical Superintendent, giving the names and addresses of 2 referees.

TAUNTON AND SOMERSET HOSPITAL. Applications are invited for the post of HOUSE OFFICER (E.N.T.). Post-registration appointment, recognised for F.R.C.S. and D.L.O.

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, Taunton and Somerset Hospital, Musgrove Park Branch, Taunton, Somerset.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. Applications invited for appointment of SENIOR ORTHOPÆDIC HOUSE SURGEON AND CASUALTY OFFICER (Senior House Officer grade) to begin duties as soon as possible. Recognised F.R.C.S. (Eng.) and tenable for 1 year. Work includes treatment of long and short stay cases and traumatic surgery with large Outpatient and Fracture Clinics under 2 Consultants.

Apply, stating age, qualifications and experience, together with 3 testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON required for post vacant 9th March. Pre-registration post.

Applications, stating age, qualifications with dates, and copies of 2 testimonials, to Secretary.

WALLASEY. VICTORIA CENTRAL HOSPITAL. Patho-LOGICAL DEPARTMENT. SENIOR HOUSE OFFICER in Pathology required. Salary £819 10s. p.a.

Applications, with details of experience and names of 3 referees, to Administrative Officer, Victoria Central Hospital, Liscard-road, Wallasey.

WARWICK (near). CENTRAL MENTAL HOSPITAL. (1400 Beds.) SENIOR HOUSE OFFICER, Neurosis Unit, Adult and Child Psychiatry Clinics, Departments of Electroencephalography, Occupational Therapy, Psychology and Social Work. Recognised for D.P.M. Accommodation available. Post vacant.

Applications, with names and addresses of 3 referees, to Medical Superintendent.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL (208 Beds.) CASUALTY OFFICER (Senior House Officer). Modern department employing 3 full-time Casualty Officers including whole-time Surgeon-in-Charge. Post recognised for F.R.C.S. Resident or non-resident. Vacant end February.

Please send applications, with names of 2 referees, to the Administrator.

WATFORD. SHRODELLS HOSPITAL. (General hos-pital—320 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to a modern Geriatric Unit of 180 Beds. Adequate time for reading. The Hospital is within reach of London teaching classes.

Applications, together with copies of 2 testimonials, should reach the Medical Administrator as soon as possible.

WELSH REGIONAL HOSPITAL BOARD. Registrar (E.N.T. surgery), Mid Glamorgan Hospital Management Committee, based Neath General Hospital, with visits to other hospitals in Group. Resident/non-resident. Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WESTON-SUPER-MARE GENERAL HOSPITAL. (104 Beds.) Applications are invited from duly qualified medical practitioners for the pre-registration appointment (resident) of HOUSE SURGEON. Immediate vacancy.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WHITEHAVEN HOSPITAL, Cumberland. (122 Beds, pre-registration post.) HOUSE PHYSICIAN (first, second or Senior House Officer post). Vacant 1st April.

Detailed applications with dates, and names of 2 referees, to Group Secretary, Workington Infirmary, Cumberland.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) SENIOR HOUSE OFFICER in Orthopædic Surgery.

Applications to Secretary, Royal Albert Edward Infirmary, Wigan.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE.

Royal Albert Edward Infirmary, Wigan
HOUSE SURGEON.

Leigh Infirmary, Leigh
HOUSE SURGEON.

Pre-registration posts.

Applications, with names of 2 referees, to Secretary, Knowsley House, Wigan.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-PITAL. (327 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant 28th February.

Applications, with copies of 2 testimonials, to Group Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. Registrar (Casualty Officer), resident, required. There is an Accident Unit of 30 Beds at the Hospital and with the Casualty Department forms part of the Accident Service for the Windsor Group and includes duties with the E.N.T. and Eye Departments. Candidates should have had previous experience in the treatment of acute injuries.

Application forms from and returnable to Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 22nd February.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) SENIOR HOUSE OFFICER (general surgery). Post vacant immediately.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) HOUSE SURGEON (pre-registration) required. Recognised for F.R.C.S. Post vacant immediately.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) HOUSE OFFICER (pre-registration) E.N.T. Department. Post recognised for the D.L.O. and F.R.C.S. examinations. Vacant 1st March.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Secretary.

WORCESTER ROYAL INFIRMARY. House Surgeon (pre-registration or otherwise) required immediately for Orthopædic Department of this busy general hospital of 213 Beds. The appointment offers wide and varied experience.

Applications to Hospital Secretary.

WORCESTER ROYAL INFIRMARY. Locum Casualty OFFICER (resident or non-resident) required in Junior Hospital Medical Officer grade, from 28th February to 13th March.

Applications to Hospital Secretary.

WORCESTER ROYAL INFIRMARY. (213 Beds.) House PHYSICIAN (paediatric) required beginning of March for busy department comprising very modern unit of 26 Beds. Post recognised for D.C.H.

Applications to Hospital Secretary.

WORTHING HOSPITAL, Lyndhurst-road, Worthing, SUSSEX. Applications are invited from registered medical practitioners for the appointment of RESIDENT CASUALTY OFFICER (Senior House Officer grade). The post is recognised for the revised Fellowship regulations in respect of the 6 months' training required by candidates for the Final Fellowship examination. Duties entail some responsibility for 52 Beds (mainly surgical) at the Hospital's recovery annexe situated 3 miles from the main hospital.

Applications, stating age, qualifications, nationality and experience, together with copies of 2 recent testimonials, to be forwarded to the Hospital Secretary, as soon as possible.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

YORK MILITARY HOSPITAL (Civilian Wing). (60 Beds.) SENIOR HOUSE OFFICER required from 8th March, 1958, resident or non-resident. There are 30 general surgical beds and 30 medical beds. The Hospital is associated with the County Hospital, a general hospital of 269 Beds, where relief casualty and emergency work and relief work for House Surgeons may be undertaken and where residence can be provided. Salary £819 10s. p.a., less £150 if resident.

Applications, stating age, nationality, experience, qualifications and names of 2 referees, to Group Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

B.W.I. UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES. Applications are invited from registered medical practitioners for the following posts:—

Vacant April:
CASUALTY OFFICER (medical). Salary £750 p.a.

Vacant July:
SENIOR CASUALTY OFFICER (surgical). Salary £850 p.a.
CASUALTY OFFICERS (medical). Salary £750 p.a.
HOUSE OFFICER (anæsthetics). Salary £750 p.a.
HOUSE OFFICER (obstetrics and gynæcology). Salary £750 p.a.

The posts are generally tenable for 6 months, although candidates recruited from outside Jamaica and for whom return passages are provided will be offered contracts for periods of 1 year covering 1 or 2 appointments. Salaries will be at the rate shown above, less a deduction of £145 p.a. for single accommodation and residence.

Further information may be obtained from the Hospital Manager and Secretary, University College Hospital of the West Indies, Mona P.O., Jamaica, B.W.I., to whom applications stating age, nationality, qualifications and experience, together with the names and addresses of 3 referees should be sent not later than 28th February, 1958.

CANADA. CHILDREN'S HOSPITAL, Vancouver, B.C. 2 PÆDIATRIC RESIDENTS required for 1-year period commencing 1st July, 1958, for 83-Bed children's acute and long-term medical and surgical hospital. 6 months' credit given by Royal College of Physicians and Surgeons of Canada toward certification in pædiatrics. Remuneration $175 per month less $20 per month accommodation. Married accommodation available.

Applications, stating age, qualifications, medical school, nationality, marital status, accompanied by recent references and photograph, should be forwarded airmail to Administrator, Children's Hospital, 250, West 59th Avenue, Vancouver, 15, British Columbia.

CANADA. REDDY MEMORIAL HOSPITAL, Westmount, MONTREAL. Graduates required as JUNIOR ROTATING INTERNES from June, 1958. Salary, $100 per month, with full board and lodging.

Apply Executive Director.

U.S.A. UNIVERSITY OF MINNESOTA MEDICAL CENTER. ANESTHESIOLOGY RESIDENCIES at the above Center. 2 or 3-year programme with clinical and didactic instruction in all phases of anæsthesia. Board approval. Positions starting every month.

Address, F. H. VANBERGEN, M.D., University of Minnesota Medical Center, Minneapolis 14, Minnesota.

Public Appointments

CORNWALL. COUNTY OF CORNWALL. Applications are invited from registered medical practitioners holding the Diploma in Public Health or its equivalent, for the mixed appointment of MEDICAL OFFICER on the staff of the County Council and MEDICAL OFFICER OF HEALTH for the undermentioned Area :—

Area II : comprising Helston Borough ; Camborne-Redruth Urban District ; Kerrier Rural District.

The salary for a mixed appointment will be on a scale of £1790 11s. 9d.–£58 14s. 4d. (3)–£36 13s. 4d. (1)–£2003 8s. 1d., which scale is in accordance with the formulæ of the Medical Whitley Council. The appointment is pensionable and the successful candidate will be required to pass a medical examination.

Further particulars may be obtained from the County Medical Officer, County Hall, Truro, to whom applications, together with 1 testimonial and the names of 2 persons to whom reference may be made, should be addressed, not later than 8th March, 1958.

E. T. VERGER, Clerk of the County Council.
County Hall, Truro, 4th February, 1958.

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
TONGUE	SUTHERLAND ..	1ST MARCH, 1958
WESTRAY	ORKNEY	1ST MARCH, 1958
OBAN	ARGYLL	1ST MARCH, 1958

BUXTON. BOROUGH OF BUXTON. URBAN DIS-TRICT OF WHALEY BRIDGE. RURAL DISTRICT OF CHAPEL-EN-LE-FRITH. DERBYSHIRE COUNTY COUNCIL. "Mixed" appointment of DISTRICT MEDICAL OFFICER OF HEALTH AND ASSISTANT COUNTY MEDICAL OFFICER. Applications are invited from registered medical practitioners (Male or Female), holding a Diploma in Public Health or equivalent qualification, for the "Mixed" appointment of Medical Officer of Health for the Borough of Buxton, the Urban District of Whaley Bridge and the Rural District of Chapel-en-le-Frith, and Assistant Medical Officer for the Derbyshire County Council. The total inclusive salary scale will be £1785 0s. 1d.–£57 14s. 6d. (3)–£60 (1)–£25 (4)–£2118 3s. 7d. p.a. The salary has been arrived at on the basis that 7/11ths of his/her time is devoted to the work of the 3 District Councils and 4/11ths to that of the County Council. As regards duties of Medical Officer of Health, the successful candidate will be subject to the sole control and direction of the District Councils, and as an Assistant County Medical Officer of Health will act under the direction of the County Medical Officer of Health who is also the Principal School Medical Officer. While there is no "divisional administration" of the County Council's medical services, he/she will be required to act as a School Medical Officer, conduct clinics and perform such other duties as may be required. Preference will be given to a candidate who has had good and varied experience in Public Health duties. The Officer will be required to live in the area of the District Councils. Sympathetic consideration will be given to the provision of temporary housing accommodation, if desired. The Officer must not engage in private practice, and must devote whole-time service to the duties of the before-mentioned posts. The appointment is subject to the provisions of the Local Government Superannuation Acts, 1937–53, and the successful candidate will be required to pass a medical examination. Canvassing, either directly or indirectly, will be a disqualification.

Application forms may be obtained from the County Medical Officer, County Offices, St. Mary's Gate, Derby. Completed forms should be sent to the Town Clerk, Town Hall, Buxton, so that they are received not later than 24th February, 1958.

SMETHWICK. COUNTY BOROUGH OF SMETHWICK. PUBLIC HEALTH DEPARTMENT. Applications are invited from registered medical practitioners for the post of ASSISTANT MEDICAL OFFICER OF HEALTH AND SCHOOL MEDICAL OFFICER. The duties will consist of work in connection with the School Health Service—including the examination and ascertainment of handicapped pupils, and Child Welfare Clinics, and opportunities will be given for the successful applicant to gain experience in special fields of public or school health work. Preference will be given to candidates who are in possession of the Diploma in Public Health or the Diploma in Child Health. If the approval of the Ministry of Education for the purpose of the ascertainment of educationally subnormal children has not previously been obtained, the successful applicant will be sent on the appropriate Course. The salary will be within the approved scale, £1050 p.a. rising by annual increments to a maximum of £1475 p.a. The post is superannuable and the successful candidate will be required to pass a medical examination. The appointment will be subject to 2 months' notice on either side. Housing accommodation may be available for the successful candidate.

Applications, stating age, qualifications and experience, and giving the names and addresses of 2 persons to whom reference may be made, should reach the Medical Officer of Health, Council House, Smethwick, not later than 5th March, 1958.

E. L. TWYCROSS, Town Clerk.
Council House, Smethwick.

WARRINGTON. COUNTY BOROUGH OF WARRING-TON. HEALTH DEPARTMENT. ASSISTANT MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER. Applications are invited from registered medical practitioners. Salary will be in accordance with national scales (£1050–£1475 p.a.). The duties will be mainly clinical in connection with maternal and child care and the school health services, but may cover any aspect of the work of the Department. The post is superannuable and subject to satisfactory medical examination.

Applications, giving details of age, qualifications and experience, together with the names of 2 referees, should be forwarded to the Medical Officer of Health, Health Department, Sankey-street, Warrington, not later than 3rd March, 1958.

ERIC H. MOORE, Medical Officer of Health,
and Principal School Medical Officer,
Health Department, Sankey-street, Warrington.
February, 1958.

GOVERNMENT OF CYPRUS. Male Medical Officer (Class 1), required mainly to attend police officers and their dependants, but will be required to perform other duties in hospital as assigned by the Director of Medical Services and possibly to act temporarily as Prison Medical Officer. Candidates should possess qualifications registrable in United Kingdom and have had considerable general practice experience. Appointment on contract for 1 tour of 21 months in first instance with gratuity (taxable) of £37 10s. a quarter. Salary including overseas allowance £1857 12s. a year. Cost-of-living allowance of 21½% of basic salary (£1548) also payable. One-half fees allowed for consulting practice outside Government hospital as institution. Government quarters if available at low rental or allowance paid in lieu. Free passages for officer, wife and children not exceeding 4 persons besides himself.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/17/07).

NAVY, ARMY AND AIR FORCE INSTITUTES. Applications are invited from general practitioners in the undernoted towns for the appointment in a part-time capacity as MEDICAL OFFICERS to the Corporation. Successful applicants would be required to examine and report on the conditions of employees of the Corporation who may be referred to them from time to time. Fees for this work will be paid on a scale agreed with the British Medical Association.

Applications, giving details of qualifications and experience, should be sent to the Chief Medical Officer, Navy, Army and Air Force Institutes, Kennington Lane, London, S.E.11, not later than 22nd February, 1958.

The towns for which applications are invited are:—

SOUTHAMPTON SALISBURY WEYMOUTH
SWINDON BOURNEMOUTH

DONEGAL COUNTY COUNCIL. Applications are invited for the post of Part-time TEMPORARY MEDICAL OFFICER to the District Hospital, Donegal. Applicants must be capable of doing major surgery. Remuneration will be at the rate of £18 2s. per week (inclusive). In addition, the person appointed will be required to perform 2 surgical sessions each week in Lifford Hospital and to be available for all emergencies there, for which he will be paid £400 p.a. inclusive, plus travelling expenses and subsistence at the approved rates. The appointment will, subject to satisfactory service, be for a period of 6 months in the first instance, which may be continued.

Applications, giving full particulars of qualifications and experience, must be lodged with the undersigned on or before 25th February, 1958. F. McKAY, Acting County Secretary.

County House, Lifford.

GOVERNMENT OF NORTHERN IRELAND. Medical OFFICERS required in Ministry of Health and Local Government for 2 pensionable posts : (1) for duties calling for experience in maternal and child welfare ; and (2) for duties involving medical inspections for purposes of Factories Acts ; supervision of persons undergoing rehabilitation courses, and clinical work in connection with industrial injury and disablement benefit schemes. Applicants should have at least 10 years experience since qualifying. Salary scale £1775 (at age 35) by annual increments to £2300, with provision for entry above the minimum. Pensions rights may in certain circumstances be transferred. Preference will be given to ex-Service candidates.

For further particulars write to Secretary, Civil Service Commission, Stormont, Belfast. Closing date 18th March, 1958.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."

BARKINGSIDE, ILFORD, ESSEX. Applications invited for death VACANCY. (Urban–intermediate area.) List approximately 3550. Not known at present whether residential and surgery accommodation will be available. Apply on Form E.C.16A by first post on 27th February, 1958, to—

E. BERGDAHL, Clerk of the Council,
Essex Executive Council, 131/3, Fillebrook-road,
Leytonstone, E.11.

LEAMINGTON SPA, WARWICKSHIRE. Applications invited for Urban VACANCY—list at present 2670. Residential and surgery accommodation available for purchase. Successful applicant to take over on 1st May, 1958. Apply on Form E.C.16A not later than 28th February, 1958.

R. V. NELLTHORP,
Clerk of the Warwickshire Executive Council.
15, Waterloo-place, Leamington Spa.

Hospital Services: Non-Medical Appointments

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. SENIOR TECHNICIAN (grade I) required for Area Laboratory at above Hospital. Experience in biochemistry an advantage though not essential. Salary £620 p.a. rising to £760 p.a. in accordance with Whitley Council scales.

Applications to Hospital Secretary, together with names of 2 referees.

BROMSGROVE, WORCESTERSHIRE. HILL TOP HOSPITAL. A post is available at the Regional Thoracic Surgical Centre at above Hospital for a BIOCHEMIST (Basic grade) in the Cardiorespiratory and Biochemistry Department.

Applications within 10 days of the appearance of this advertisement, together with the names of 2 referees, should be sent to the Hospital Secretary, from whom further information may be obtained.

Miscellaneous

John Wyeth & Brother Limited. Applications are invited for the full-time post of Medical Adviser. Responsibilities of this post include : the arrangement of clinical investigations ; cooperation in research and the development of new therapeutic agents ; advising the Company and members of the medical profession as the need arises, and assisting in the training of representatives. Close contact with current medical matters from both theoretical and practical aspects is essential. Candidates should have the ability to occupy the highest grades of the profession, either in general or hospital practice, and the salary will be in the range of £1750–£2250 according to age and experience.—Applications should be received by 1st March, 1958, by the Medical Director at Clifton House, Euston-road, London, N.W.1.

Required. Research worker holding degree in psychology, at the Burden Neurological Institute.—Apply, stating academic status and research experience, to Director, Burden Institute, Stoke-lane, Stapleton, Bristol.

GROUP MEDICAL OFFICER

The Industrial Group of
THE UNITED KINGDOM ATOMIC ENERGY AUTHORITY
has a vacancy in the
Medical Division of the
HEALTH AND SAFETY BRANCH

at its Headquarters at Risley, Warrington, Lancashire, for a Group Medical Officer who will be responsible to the Director of Health and Safety for the administration of the medical arrangements of the Group, in relation, for example, to medical examinations, facilities for treatment and laboratory services ; and he will also be responsible for the application in detail of standards of radiation exposure recommended by the Medical Research Council for the control of radiation hazards.

At each Works of the Industrial Group there is a Works Medical Staff for whom the Group Medical Officer will be functionally responsible.

Applications are invited from suitably qualified medical practitioners, who have had training and experience in industrial medicine. A knowledge of the biological aspects of radiological protection and experience in medical administration would be an advantage.

This is a senior professional appointment and will carry a substantial salary commensurate with the ability, experience and qualifications required.

The post is permanent and pensionable. Housing should be available within a reasonable time.

Apply to : Chief Recruitment Officer, U.K.A.E.A., Industrial Group Headquarters, Risley, Warrington, Lancashire.

Please quote reference 2262.

Closing date : 3rd March, 1958.

THE ROYAL NETHERLANDS FERMENTATION INDUSTRIES LTD.,

a major producer of yeast, antibiotics and pharmaceuticals at Delft, Holland, has a vacancy in its research division for the position of:—

HEAD OF THE PHARMACOLOGICAL AND TOXICOLOGICAL DEPARTMENT

We like this very responsible position to be filled by a university graduate with research experience and interests.

A position for life with attractive research possibilities for a young pharmacologist.

Replies, please, direct to: Management Royal Netherlands Fermentation Industries Ltd., Wateringseweg 1, Delft, Holland.

Canada. Ophthalmologist wanted with view to early partnership. Salary $10,000 first year or mutually agreed alternative.—Send full particulars Address No. 371, THE LANCET office, 7, Adam-street, Adelphi, London, W.C.2.

General Practice. Near Christchurch, New Zealand. £2000 p.a. for 3 years guaranteed by local residents. Modern house and surgery available. £3000 mortgage transferable. £1650 secures house and practice.—Address, No. 372, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC 0141), who are specialists.

Duplicating. Specialists in medical terminology. Prompt service. All work strictly confidential.—HOPKINS LTD., 61, St. Helena-street, W.C.1. TERminus 2284.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

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Required. Lancet, Vol. II, 1915; Vols. I and II, 1916–1918; Vol. I, 1919.—Replies stating condition and price to Address, No. 373, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Expert medico-legal photographic service. Accident, injury, claims. Any location.—Address, No. 370, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2, or PEGGY DELIUS, WEL. 7788.

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Are also the most effective."—Hippocrates

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New Era in Diuretic Therapy

For the first time, there is available a non-mercurial diuretic agent which, when administered ORALLY, is usually completely free from side-effects, has no known contra-indications, and is effective in the treatment of oedema of all degrees of severity—often when ALL other diuretics have failed.

This agent is 'SALURIC' *(Chlorothiazide)* discovered in the Merck Sharp & Dohme Research Laboratories.

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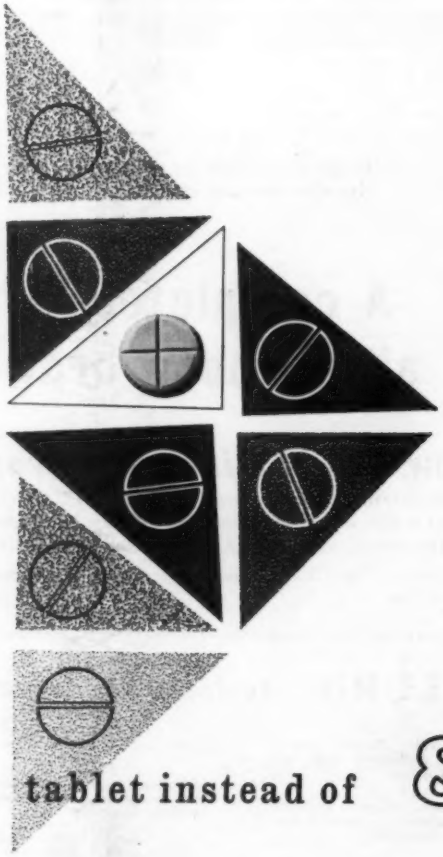

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